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ENVIRONMENT AND WATER RESOURCES

WATER QUALITY GUIDELINES FOR SULFOLANE

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EXECUTIVE SUMMARY

Introduction

Sulfolane is an organic chemical used for a wide variety of industrial purposes. The primary industries that use sulfolane include natural gas processing, plastics, and electronics. Environmental quality guidelines have not been developed for sulfolane by federal or provincial agencies in Canada.

This report presents proposed water quality guidelines for sulfolane for the province of British Columbia. This work was completed by Komex International Ltd. under contract #WMB 02-060 ("the Contract") to the British Columbia Ministry of Water, Land and Air Protection, Water Management Branch. The guidelines were developed using protocols published by the Canadian Council of Ministers of the Environment (CCME), where applicable, referred to herein as "the Protocol". The guidelines are numerical limits for contaminants in water intended to maintain, improve, or protect environmental quality and human health. Water quality guidelines were developed for freshwater aquatic life, irrigation, livestock watering, and source water for drinking.

An extensive literature search was conducted to identify toxicity data for sulfolane to mammals, and aquatic, terrestrial, and microbial organisms. Critical data gaps were identified and the following work was commissioned:

- sulfolane toxicological testing of four plant species in four soil types (Scientific Information Services);
- sulfolane toxicological testing of one cold water fish species (rainbow trout) and one freshwater invertebrate (sideswimmer) (Environment Canada Pacific Environmental Service Centre);
- a comprehensive review of mammalian toxicology studies for sulfolane, and derivation of tolerable daily intakes (Cantox Inc.); and,
- a subchronic study of the oral toxicity of sulfolane to rats (Huntingdon Life Sciences).

Sulfolane Water Quality Guidelines

Sulfolane is a colourless, highly polar, water-soluble compound with exceptional chemical and thermal stability and unusual solvent properties. Sulfolane has traditionally been used in the extraction of aromatics from hydrocarbon mixtures and in sour gas sweetening, (*i.e.,* removal of acid gases from a natural gas stream). Due to its combination of physical and chemical properties, sulfolane has been used in a variety of new applications including as an extraction distillation solvent, polymer solvent, polymer plasticizer, polymerization solvent, and in

electronic/electrical applications. Sulfolane is highly mobile in the subsurface, migrating at close to groundwater flow velocity. Biodegradation under typical aquifer conditions can be very slow.

Recommended guidelines for freshwater aquatic life, irrigation, livestock watering, and source water for drinking are summarized in Table 3.1.

Freshwater Aquatic Life

The Interim guideline for freshwater aquatic life was calculated to be 50 mg L^{-1}.

Irrigation

Four Interim guidelines were calculated for irrigation. Based on the Protocol, guidelines were calculated for: 1) cereals, tame hays, and pasture crops; and, 2) other crops. For each of these two groups of plants, guidelines were calculated for two soil types: 1) loam; and, 2) the soil that gave the most sensitive response from any plant in the toxicity testing ("poor soil"). The guidelines for cereals, tame hays, and pasture crops were 95 mg L^{-1} (loam), and 42 mg L^{-1} (poor soil). For other crops it was 38 mg L^{-1} (loam), and 8.4 mg L^{-1} (poor soil). The overall Interim irrigation guideline was 8.4 mg/L.

Livestock Watering

Preliminary guidelines for this water use were calculated for dairy cattle, beef cattle, and deer, to represent likely agricultural and wild animals. The most sensitive species was the dairy cow, for which a guideline of 14 mg L^{-1} was calculated. It should be noted that these guidelines were based on studies with laboratory animals using appropriate safety factors; no toxicological information was available for livestock species (either mammalian or avian). Should such data become available in the future, this guideline could be refined.

Source Water for Drinking

Interim source water for drinking guidelines were calculated for children (0.27 mg L^{-1}) and adults (0.46 mg L^{-1}).

Data Gaps

Data gaps were identified in the toxicological dataset for sulfolane, and are discussed in the main text. Overall, the data gaps for this compound are relatively minor. It is felt that the presently available toxicological dataset and the guidelines presented in this document provide a consistent picture of the toxicity of this compound.

1. INTRODUCTION

This report presents proposed water quality guidelines for sulfolane for the province of British Columbia. This work was completed by Komex International Ltd. under contract #WMB 02-060 ("the Contract") to the British Columbia Ministry of Water, Land and Air Protection, Water Management Branch. The sulfolane water quality guidelines presented in this document are based on a project conducted by the Canadian Association of Petroleum Producers (CAPP, 2001) to determine soil and water environmental quality guidelines for sulfolane and diisopropanolamine (DIPA). Further, detailed information is available in CAPP (2001), and reference is made to this document where appropriate.

1.1 Scope of Work

The scope of work for this document included the following tasks:

- review and summarize relevant available background information on sulfolane;
- review and summarize the environmental fate and behaviour of sulfolane;
- review and summarize available information on the toxicity of sulfolane;
- conduct a critical review of data gaps and commission additional toxicity work as required;
- develop tolerable daily intakes (TDIs) of sulfolane for humans and livestock (CanTox Inc.); and,
- derive water quality guidelines for sulfolane using applicable (Canadian Council of Ministers of the Environment (CCME)) protocols for freshwater aquatic life, irrigation, livestock watering, and source water for drinking.

1.2 Background

Sulfolane is an organic chemical used for a wide variety of industrial purposes. The primary use of sulfolane is in the "sweetening" (*i.e.*, removal of acid gasses) from natural gas streams. Other industries that use sulfolane include plastics and electronics. Despite its wide use, however, federal or provincial environmental quality guidelines have not been developed for this chemical.

1.3 Protocols

Environmental quality guidelines for sulfolane were developed using the following protocols developed by the CCME:

A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life. (CCME, 1999).

Protocols for Deriving Water Quality Guidelines for the Protection of Agricultural Water Uses. (CCME, 1999).

For ease of reference in this document, the phrase "the Protocol" refers to whichever of the above documents is applicable. For instance, in the section on developing freshwater aquatic life guidelines, "the Protocol" would refer to CCME (1999) *A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life.* Note that the Aquatic Life and Agricultural Water Uses Protocols listed above were originally published as CCME (1991), and CCME (1993), respectively, and were reproduced with minor changes in CCME (1999).

Source water for drinking guidelines were developed using standard risk assessment algorithms and protocols (US EPA, 1989; CCME, 1996). Toxicology work commissioned for CAPP (2001) was performed under applicable Environment Canada protocols.

1.4 Toxicity Data

An extensive literature search was conducted to identify toxicity data for sulfolane to mammals, and aquatic, terrestrial, and microbial organisms. Critical data gaps were identified and the following work was commissioned:

- sulfolane toxicological testing of four plant species in four soil types (Scientific Information Services);
- sulfolane toxicological testing of one cold water fish species (rainbow trout) and one freshwater invertebrate (sideswimmer) (Environment Canada Pacific Environmental Service Centre);
- a comprehensive review of mammalian toxicology studies for sulfolane, and derivation of tolerable daily intakes (Cantox Inc.); and,
- a subchronic study of the oral toxicity of sulfolane to rats (Huntingdon Life Sciences).

2. BACKGROUND INFORMATION

2.1 Physical and Chemical Properties

Sulfolane [126-33-0], $C_4H_8SO_2$, is known under a variety of synonyms and trade names (Table 2.1).

Sulfolane was first described in the chemical literature in 1916 (Kirk-Othmer, 1999). Based on its chemical and thermal stability and solvent properties, research into commercial processes of sulfolane production commenced in approximately 1940. In 1959, sulfolane production reached levels sufficient for broader uses. Since then, the uses and applications of sulfolane have significantly increased.

Published physical and chemical properties are summarized in Table 2.2. Sulfolane is a colourless, highly polar, water-soluble compound with exceptional chemical and thermal stability and unusual solvent properties.

2.2 Analytical Methods

There are currently no recommended methods for sulfolane analysis published by CCME or the US EPA. Generally, sulfolane analysis can be conducted by direct injection or solvent extraction, gas chromatographic (GC) separation, and detection by flame ionization, mass-selective, or electrolytic conductivity.

Analytical methods for sulfolane in aqueous supernatants from biodegradation studies were described in the scientific literature. Chou and Swatloski (1983) analyzed sulfolane by GC and using a packed column, but did not further specify analytical procedures. McLeod *et al.* (1992) extracted sulfolane from acidified water samples with dichloromethane and analyzed the extract by GC with a flame ionization detector (FID). CAPP (1997), Greene *et al.* (1998), Gieg *et al.* (1998), Luther *et al.* (1998), Gieg *et al.* (1999), and Greene *et al.* (1999) analyzed aqueous supernatants from laboratory cultures of biodegradation microcosm studies. Described methods involve direct injection and the use of a GC equipped with a FID. Reported detection limits varied between 0.5 and 5 mg L^{-1}, depending on the GC used.

Headley *et al.* (1999a, 1999b) described a gas chromatography-mass spectrometry (GC-MS) method for analysis of sulfolane in vegetation samples of a sulfolane-contaminated wetland. Sample preparation included grinding and homogenizing frozen vegetation samples under liquid nitrogen. Ground samples were transferred into centrifuge tubes and allowed to warm to room temperature. Following addition of deionized water and equilibration for 45 minutes, samples were centrifuged for 45 minutes at 2,500 rpm. The supernatants were then filtered and transferred into a centrifuge tube. Supernatants were back-extracted serially with water-saturated toluene and analyzed by liquid chromatography-mass spectrometry-mass spectrometry (LC-MS-MS).

Analytical methods used by two commercial laboratories that routinely conduct environmental sulfolane analysis of water and soil samples are summarized below:

One laboratory saturates water samples with NaCl and extracts sulfolane with ethyl ether/dichloromethane. Soil samples are extracted by Soxhlet extraction using dichloromethane. The extracts are analyzed by GC and sulfolane detection is achieved using a mass-selective detector in the selected ion monitoring mode. Detection limits are 0.001 mg L^{-1} and 0.05 mg kg^{-1} for water and soil, respectively.

The other commercial laboratory uses a direct injection, GC-FID technique for water samples with sulfolane concentrations exceeding 2 mg L^{-1}. Water samples containing sulfolane concentrations of less than 2 mg L^{-1} are pre-concentrated using an extraction with a medium polarity solvent and extract concentration by evaporation. Soil samples are extracted with deionized water and are pretreated with a non-polar solvent if the soil sample contains significant concentrations of petroleum hydrocarbons. Samples or extracts are analyzed by GC using a polar column and an electrolytic conductivity detector operating in the sulphur-specific mode. Detection limits are 0.001 mg L^{-1} and 0.01 to 1 mg kg^{-1} for water and soil, respectively.

The accuracy, precision, and Type I and Type II errors associated with sulfolane water analyses conducted by the second commercial laboratory were investigated by Komex International Ltd. (Komex) in 1995 and 1998 (Komex, 1999). The accuracy at sulfolane spike concentrations of 5, 10, and 50 µg L^{-1} ranged between 10 and 21%. Mean measured concentrations showed a positive bias (*i.e.*, measured value was higher than spike concentration) for nine out of twelve results. Sulfolane accuracy was not adversely affected by a matrix of local river water relative to a matrix of deionized water. Precision ranged from 0 to 66%, with an average precision of 22%.

Blanks and matrix blanks yielded results below the detection limit (<0.001 mg L^{-1}), indicating no false positives (Type I errors) were obtained. All spikes and matrix spikes returned measurable concentrations indicating no false negatives (Type II errors) were obtained.

2.3 Production and Uses

2.3.1 Production

Industrially, sulfolane is synthesized by hydrogenation of 3-sulfolene ($C_4H_6SO_2$), which is prepared through the reaction of butadiene (C_4H_6) and sulphur dioxide (SO_2). The reaction path is shown below:

$$C_4H_6 + SO_2 \rightarrow C_4H_6SO_2 \qquad \text{and} \qquad C_4H_6SO_2 + H_2 \rightarrow C_4H_8SO_2$$

Sulfolane manufacturing using butadiene and sulphur dioxide was patented by Shell in 1944 (Morris and Shokal, 1944). In 1951, sulfolane preparation by catalytic hydrogenation of sulfolene oxides was patented by Phillip Petroleum (Mahan and Fauske, 1951).

In North America, sulfolane is produced by Phillips Chemical Company (Borger, Texas, USA). Inspec Fine Chemicals Limited (United Kingdom) indicates they are the world's largest and the only European sulfolane manufacturer. According to Phillips Chemical Company, smaller producers of sulfolane in China and India have begun production within the last few years. The total worldwide production of sulfolane was estimated between 18,000 and 36,000 tons per year (approximately 6.4×10^6 to 12.0×10^7 L). Commercially, sulfolane is available as anhydrous sulfolane and as sulfolane containing 3% (wt.) deionized water.

2.3.2 Uses

Sulfolane has been traditionally used in the extraction of aromatics and in sour gas sweetening, (*i.e.,* removal of acid gases from a natural gas stream). Due to its combination of physical and chemical properties, sulfolane has been used in a variety of new applications including as an extraction distillation solvent, polymer solvent, polymer plasticizer, polymerization solvent, and in electronic/electrical applications. Commercial and industrial uses of sulfolane have been discussed in Kirk-Othmer (1999) and are summarized below.

2.3.2.1 Extractive Solvent

Sulfolane is dominantly used as an extraction solvent of benzene, toluene, and xylene from aliphatic hydrocarbon mixtures (Kirk-Othmer, 1999). This process is referred to as BTX processing (Beardmore and Kosters, 1963; Broughton and Asselin, 1968; Plummer, 1973; Plummer, 1980) and was introduced in 1959 by the Shell Development Company. The BTX process is licensed by Universal Oil Products. BTX processing involves sulfolane extraction of aromatic and some light non-aromatic hydrocarbons from the hydrocarbon feed. The non-aromatic fraction is subsequently stripped in an extractive stripper. The aromatic fraction is removed from the sulfolane solvent using a recovery column. In 1994, worldwide consumption was estimated at approximately 6,974 tons per year of sulfolane for 137 extraction units (Kirk-Othmer, 1999).

In addition, sulfolane is used as extractive solvent for normal and branched aliphatic hydrocarbons (Little, 1971; Hanson, 1972), fatty acids, and fatty acid esters (Morris and Shokal, 1944; Wisniak, 1970; Cloughley *et al.*, 1993). In the latter process, sulfolane is used to enrich the unsaturation level of animal and vegetable fatty oil for use in paints, synthetic resins, food products, plastics, and soaps. Sulfolane is further used in a wood delignification process in

which sulfolane extracts the lignin from wood chips thereby freeing the cellulose fibers (Clermont, 1970; Starr *et al.*, 1975).

Further extractive solvent applications include removing mercaptans and sulfides from sour petroleum (Agrawal *et al.*, 1987), removing t-butylstyrene from t-butylethylbenzene (Henery *et al.*, 1985), removing mixtures of close-boiling chlorosilanes (Marko and Rentsch, 1983) and removing aromatics from kerosene (Jain and Chopra, 1991; Joshi *et al.*, 1992; Khanna and Rawat, 1992), naphtha (Krishna *et al.*, 1987; Fandary *et al.*, 1989; Poposka *et al.*, 1991; Khanna and Rawat, 1992), and aviation fuel (Mehrotra *et al.*, 1986).

2.3.2.2 Gas Treating

Sulfolane is used as solvent in the Sulfinol process to remove acid gases from natural gas. The Sulfinol process was introduced by Shell in 1963 and consists of passing the natural sour gas stream through a mixture of sulfolane, diisopropanolamine (DIPA), or methyldiethanolamine, and water (*e.g.*, Dunn, 1964; Fisch, 1977; Yogish, 1990; MacGregor and Mather, 1991; Murrieta-Guevarra *et al.*, 1994;). Acid gases including hydrogen sulphide (H_2S), carbon dioxide (CO_2), carbonyl sulphide (COS), carbon disulphide (CS_2), and mercaptans (thiols) are physically absorbed by sulfolane and chemically absorbed by DIPA thereby "sweetening" the gas stream.

Sulfolane is used for other gas treatment processes including:

- hydrogen selenide removal from gasification of coal, shale, or tarsands (Baker, 1988);
- olefin removal from alkanes (Mehra, 1987a);
- nitrogen, helium, and argon removal from natural gas (Mehra, 1987b);
- atmospheric CO_2 removal in nuclear submarines;
- ammonia and H_2S removal from waste streams;
- H_2S, HCl, N_2O, and CO_2 removal from various streams (*e.g.*, Mather and Roberts, 1988; Mather *et al.*, 1991; Mather and Li, 1994); and,
- H_2S and SO_2 removal from gas mixtures (Gustafson and Miller, 1969; Hettick and Little, 1970; Schulze, 1972), which differs from the Sulfinol process in that H_2S and SO_2 are converted directly to elemental sulphur.

2.3.2.3 Extractive Distillation Solvent

Sulfolane is used for separating components in narrow boiling range mixtures such as alcohols (Lee *et al.*, 1992), chlorosilanes (Flaningham and Halm, 1983; Halm and Rentsch, 1983), mono- and diolefins such as isoprene and butadiene (Lee and Brown, 1992), electrochemical fluorination products, water from organic acids (Berg and Yeh, 1987; Berg and Yeh, 1988; Berg, 1992a; Berg, 1992b), ethers (*e.g.*, Berg and Yeh, 1984a; 1984b), ketones (Berg and Bentu,

1990a; 1990b), esters (Berg and Wytcherley, 1993), cycloalkanes from alkanes (Lee, 1990), and aromatic hydrocarbons (*e.g.*, Rawat *et al.*, 1972; Lee and Coombs, 1987).

2.3.2.4 Polymer Solvent

Sulfolane is used as a solvent in a variety of polymers including polyacrylonitrile (PAN), poly(vinylide cyanide), poly(vinyl chloride) (PVC), poly(vinyl fluoride), and polysulfones (Miller, 1951; Heisenberg and Kleine, 1952; Rothrock, 1955; Barton, 1960; Little, 1969; Covitch and Sweetapple, 1985).

2.3.2.5 Polymer Plasticizer

Sulfolane is used to plasticize nylon, cellulose, and cellulose esters to improve flexibility and increase elongation of the polymer (Hooker and Peterson, 1949; Garrison and Hyde, 1968). Sulfolane is further utilized for the synthesis of cellulose hollow fibers as permeability membranes in reverse osmosis cells (Hooker and Peterson, 1949; Davis and Skiens, 1971; Schrader, 1971).

2.3.2.6 Polymerization Solvent

Sulfolane has been used alone or in combination with a co-solvent as a polymerization solvent for polyureas, polysulfones, polysiloxanes, polyether polyols, polybenzimidazoles, polyphenylene ethers, poly(1,4-benzamide), poly(imino-1,4-phenylenecarbonyl), silylated poly(amides), poly(arylene ether ketones), polythioamides, and poly(vinylnaphthalene/fumaronitrile) (Kirk-Othmer, 1999). The use of sulfolane is based on increased polymerization rate, ease of polymer purification, better solubilizing characteristics, and improved thermal stability.

2.3.2.7 Electronic and Electrical Applications

Sulfolane has been tested as the solvent in lithium batteries due to its high dielectric constant, low volatility, solubilizing characteristics, and aprotic nature (*e.g.*, Blomgren, 1980; Matsuda *et al.*, 1985; Koch *et al.*, 1987; Maxfield *et al.*, 1989; Visco *et al.*, 1990). Sulfolane has also been patented for use as a coil-insulating component, solvent in electronic display devices, as capacitor impregnant, and as a solvent in electroplating baths (*e.g.*, Huba and Bride, 1972; Wisenberg, 1975; Reddy, 1978; Versberg, 1978).

2.3.2.8 Miscellaneous Uses

Miscellaneous uses of sulfolane include the textile industry for preparation of dyes, fabric treating prior to dyeing, and fiber treating (Roberts, 1972; Dawson and Schofield, 1974; Ono *et*

al., 1977); curing of polysulphide-based sealants and fluoropolymer rubbers (Kolb, 1975; Miller, 1978); use as catalyst (Onsager, 1973; Kawaguchi, 1974); detoxification of pesticides and chemical warfare agents (Seiders, 1985); and co-surfactant in systems for enhanced petroleum recovery (Stapp, 1984).

2.4 Levels in the Canadian Environment

The occurrence of sulfolane in the environment has been reported in groundwater, surface water, soil, and plants in the vicinity of facilities where it has been used. It is anticipated, however, that in environments located away from such facilities (*i.e.*, most of Canada) sulfolane will not be present at measurable concentrations.

Reports on the presence of anthropogenic sulfolane in the environment are limited to data collected at three sour gas processing facilities in Alberta and British Columbia (CAPP, 1997; Wrubleski and Drury, 1997). At these facilities, a maximum soil sulfolane concentration of 701 mg kg^{-1} was measured in clay-rich till. Maximum measured sulfolane concentrations in groundwater, collected from contaminated aquifers beneath one of the gas processing facilities, were 88 mg L^{-1} in a bedrock aquifer and 800 mg L^{-1} in a shallow till aquifer (Gieg *et al.*, 1998). At one of the facilities, sulfolane-impacted groundwater discharged via a wetland into a creek. Levels within the wetland and the creek were significantly reduced compared to the discharging groundwater. Maximum sulfolane concentrations reported in groundwater and creek water were 800 and 0.4 mg L^{-1}, respectively.

Sulfolane uptake by wetland vegetation was studied as part of a CAPP research program to evaluate natural attenuation processes in contaminated wetlands (CAPP, 1998; 1999; 2000). Roots, stems, leaves, flower heads, seed heads, and berries of cattail, dogwood, sedge, marsh reed grass, cow parsnip, and smooth brome growing in a sulfolane-impacted wetland were included in the study (CAPP, 1999 and 2000; Headley *et al.*, 1999a). Analytical results indicated highly variable sulfolane concentrations for different parts of the same species (*e.g.*, roots versus leaves), between different plant species (*e.g.*, cattail leaves versus sedge leaves), and even between different samples of the same part of the same species. The maximum measured sulfolane concentration in plants from the wetland was 256 mg kg^{-1}. The maximum measured sulfolane concentration in water within the wetland was 185 mg L^{-1}.

The only report of sulfolane occurring naturally in the environment was published by Barrow and Capon (1992). The authors identified sulfolane in a composite sample of a sponge (*Batzella*) and tunicate (*Lissoclinum*). The specimens contained approximately 50 mg (kg dry weight)$^{-1}$ sulfolane.

2.5 Existing Guidelines and Criteria in Various Media

Federal or provincial environmental quality guidelines have not been developed for sulfolane.

2.6 Environmental Fate and Behavior

The fate and behavior of a compound released to the subsurface environment is determined by the physical and chemical properties of the compound and the attenuation processes (including biodegradation) to which it is subjected. The relationship between compound properties, and fate and behavior can be used to predict the potential for the persistence and transport of sulfolane in the environment. Physical and chemical properties of sulfolane (Table 2.2) in combination with recently published sorption studies are discussed in the sections below to evaluate the environmental fate and behavior of sulfolane.

2.6.1 Adsorption and Mobility

Sulfolane sorption parameters were investigated in batch equilibration studies by Luther *et al.* (1998) (Table 2.2). Sorbent materials included aquifer sediments from sulfolane-contaminated sour gas treatment facilities, reference montmorillonite and kaolinite clays, and six soils of various clay and organic matter contents. Sulfolane sorption isotherms were found to be linear. Sorption by aquifer materials was reported to be very low with an aqueous phase sediment partitioning coefficient (K_d) of less than 1 L kg^{-1}. The sulfolane K_d for clay minerals (0.18 to 0.94 L kg^{-1}) was higher than for humus-rich soil (0.099 L kg^{-1}). Cation exchange capacity (CEC) was found to be a reasonable predictor of sulfolane sorption by soils and aquifer materials with low organic carbon content (*i.e.*, <1%).

Sulfolane retardation coefficients calculated by Luther *et al.* (1998) for aquifer sediments were reported for weathered sandstone (1.0), weathered shale/sandstone (1.3), and clay-rich till (1.5). These values indicate sulfolane will migrate at a similar velocity to the groundwater flow.

The organic carbon-water partition coefficient (K_{oc}) and the *n*-octanol-water partition coefficient (K_{ow}) represent the equilibrium ratio of sulfolane sorbed by organic carbon or in octanol to its concentration in water, respectively, and are reported in Table 2.2. The low K_{oc}, low K_{ow}, high pKa (negative logarithm of the acid dissociation constant) values, and high water solubility of sulfolane are consistent with the findings of the sulfolane sorption study summarized above and indicate there is a low potential for sulfolane to sorb to sediments or soils. Thus, sulfolane is predicted to be highly mobile in the subsurface.

2.6.2 Aqueous-Phase Solubility

Sulfolane is highly water soluble and considered miscible at 25° C (Table 2.2). Its pKa value of 12.9 (Table 2.2) indicates sulfolane is a neutral molecule in the most commonly observed subsurface environments with pH values between 6 and 8.

2.6.3 Leaching and Lateral Movement

The leaching and lateral movement potential of sulfolane is determined by its low affinity for sorption, low retardation coefficients in sulfolane-contaminated aquifer sediments, and high solubility. CAPP (1997) used the classification system of McCall *et al.* (1980) to classify sulfolane mobility as very high. Thus, sulfolane is predicted to partition into water migrating downward through the vadose (*i.e.,* unsaturated) zone. Once in the saturated zone, the migration rate of sulfolane is likely a function of the hydraulic conductivity of the aquifer material, the hydraulic gradient, and the susceptibility of sulfolane to biological attenuation processes (*i.e.,* biodegradation).

2.6.4 Biodegradation

The biodegradation of sulfolane has been investigated in an activated sludge system, in wastewater treatment, in laboratory microcosm studies using contaminated aquifer sediments, and as part of a natural attenuation study in natural wetlands. Most studies have demonstrated that sulfolane biodegrades in nutrient-enriched aerobic microcosms from a variety of sulfolane-contaminated environmental samples. Published sulfolane biodegradation rates and lag times (*i.e.,* time required before degradation starts) are highly variable. Biodegradation rates range from 0 to 330 mg L^{-1} day^{-1}. Lag times range from <1 to 220 days (Table 2.3).

The ability to degrade sulfolane in refinery wastewater and groundwater using activated sludge or biologically activated carbon was investigated by Bridié *et al.* (1979b), Chou and Swatloski (1983), Bagnall *et al.* (1984), Juhl and Clark (1990), McLeod *et al.* (1992), and Tian (1992). The findings of these studies were summarized by Witzaney and Fedorak (1996). The aerobic degradation of sulfolane by an activated sludge system was associated with a significant drop in pH (Chou and Swatloski, 1983). In an unbuffered system, a pH decrease from 7 to 4.5 and 5 occurred after degradation of approximately 10% of the sulfolane present. The complete oxidation of sulfolane was given by Greene *et al.* (1999) as:

$$C_4H_8O_2S + 6.5O_2 \rightarrow 4CO_2 + 3H_2O + 2H^+ + SO_4^{2-}$$

Thus, the release of H_2SO_4, a strong acid, causes the observed drop in pH which resulted in termination of the microbial activity in the Chou and Swatloski (1983) study.

Salanitro and Langston (1988) conducted biodegradation studies on soil microcosms in response to a Sulfinol spill. Their findings are summarized in Table 2.3.

A number of recent studies have investigated sulfolane biodegradation using nutrient-amended and -unamended microcosms, under aerobic and anaerobic conditions, and at temperatures ranging from 8° to 28° C. Microcosm studies were conducted using sediments and soils from sulfolane contaminated aquifers. Aquifer materials ranged from sandstone, to till and sand, to wetland sediments. Materials, conditions, lag times and biodegradation rates reported in microcosm studies are summarized in Table 2.3.

Greene *et al.* (1998) conducted aerobic and anaerobic microcosm studies at 8° and 28° C using a variety of sediments from contaminated aquifers. This study documented aerobic sulfolane degradation at 8° and 28° C under addition of the appropriate nutrients such as nitrogen and phosphate. Under aerobic conditions, nearly complete sulfolane removal occurred within 2 to 4 days at 28° C and within 8 to 12 days at 8° C. Results confirmed that previous exposure of aquifer materials to sulfolane and supplementing microcosms with nitrogen and phosphate (Fedorak and Coy, 1996) enriches a microbial community, resulting in more rapid sulfolane degradation. Kinetic analyses indicated that sulfolane degradation is more accurately described by zero-order than first-order kinetics. Under anaerobic conditions, no evidence of sulfolane biodegradation was observed at 28° C or under Fe^{3+}, SO_4^{2-}, and CO_2 reducing conditions at 8° C. In a limited number of microcosms, evidence for biodegradation was observed under Mn^{4+} and NO_3^- reducing conditions. Thus, Greene *et al.* (1998) concluded sulfolane biodegradation would not be significant in anaerobic aquifers.

Aerobic microcosm studies conducted at 8° C using sediments and groundwater from sulfolane-contaminated aquifer materials and background locations confirmed the presence of sulfolane degraders in all contaminated samples (Greene *et al.*, 1999). Previously uncontaminated samples were able do degrade sulfolane, but the lag time before degradation started was typically longer, and the degradation rate was typically slower than with previously contaminated samples. This suggests that soil bacteria exposed to sulfolane adapt over time to be able to degrade sulfolane. Sulfolane biodegradation in previously contaminated aquifer materials was greatly enhanced by the addition of phosphate, whereas the addition of nitrogen yielded little stimulation. Once commenced, sulfolane degradation continued to levels below the detection limit (<1 mg L^{-1}).

The only metabolite detected in microbial cultures was reported to be sulphate (Chou and Swatloski, 1983). They further hypothesized that sulfolane degradation may produce butyrate, a fatty acid. Other metabolites of sulfolane have not been identified to date. Bressler *et al.* (1999) reviewed the biodegradation of sulphur-heterocycles and suggested the cleavage of the sulfolane ring is most likely to occur by breaking a C-S bond. The metabolite produced would probably be a four-carbon sulfinic acid (CAPP, 1997). Based on evidence from the microcosm studies referenced above, during biodegradation of sulfolane nearly stoichiometric amounts of sulphur are released as sulphate. Hence, the C-S bond in the hypothesized sulfinic acid metabolite must be cleaved. If no C-C bonds are broken before the second C-S cleavage, an oxidized metabolite

containing four C atoms would be formed. If one or more C-C bonds are broken before the second cleavage of a C-S bond, oxidized metabolites containing less than four C atoms would be formed. CAPP (1997) suggested that these hypothesized metabolites would be susceptible to further degradation and predicted sulfolane biodegradation should not generate an accumulation of organic carbon in the medium, except for biomass.

2.6.5 Volatilization

Volatilization potential is commonly expressed using the vapour pressure and the Henry's law constant of a compound. The Henry's law constant is the equilibrium ratio of the concentration in the gas phase to the concentration in the aqueous phase. This value is closely related to the vapour pressure of a compound, but is also dependent on its aqueous solubility and molecular weight and, therefore, can be used to make a more accurate prediction of volatility than one based on solely on vapour pressure.

Lyman *et al.* (1982) used Henry's law constants to classify volatilization potential as follows:

- values less than 10^{-7} atm m^3 mol^{-1} indicate the substance is less volatile than water and can be considered essentially non-volatile;
- values between 10^{-7} and 10^{-5} atm m^3 mol^{-1} indicate the substance may volatilize slowly but the compound will still tend to partition into the aqueous phase;
- values between 10^{-5} and 10^{-3} atm m^3 mol^{-1} indicate volatilization is significant; and,
- values greater than 10^{-3} atm m^3 mol^{-1} indicate the majority of the mass of the compound will tend to partition into the gas phase.

The vapour pressure of a compound is the pressure that the vapour phase of a compound exerts at equilibrium with its aqueous phase. Vapour pressures are reported for a given temperature and increase with increasing temperature. Compounds with high vapour pressures are more likely to volatilize than those with lower vapour pressures. Thus, the potential of vapour-phase transport of a compound increases with increasing vapour pressures.

The very low Henry's law constant of sulfolane (8.9×10^{-10} atm m^3 mol^{-1}), combined with a low vapour pressure (Table 2.2), suggest sulfolane can be considered essentially non-volatile. Thus, vapour-phase transport in the vadose zone is not expected to be significant.

2.6.6 Photolysis

No information on the susceptibility of sulfolane to phototransformation reactions was available at the time this report was prepared.

2.7 Behavior and Effects in Terrestrial Biota

2.7.1 Terrestrial Plants

The toxicity of sulfolane to terrestrial plants is summarized in Table 2.4. Two toxicity studies have been completed. Data for both studies are provided in CAPP (2001).

The first study (Komex, 1999) conducted on lettuce (*Lactuca sativa)*, consisted of a five day seed germination/root elongation test. This is a widely used and accepted short-term test for plants (*e.g.*, Ratsch and Johndro, 1986; Wang, 1987; Wang and Williams, 1988; ASTM, 1990). Komex (1999) reported LOEC values of 570 mg kg^{-1} (root elongation) and 1,200 mg kg^{-1} (seed germination) for lettuce (*Lactuca sativa*) grown in a fine-textured soil (Table 2.4).

The second terrestrial plant toxicity study (CAPP, 2001), was conducted by Scientific Information Services using an Environment Canada (1998) draft protocol, four plant species (lettuce (*Lactuca sativa),* carrot *(Daucus carota),* alfalfa *(Medicago sativa),* and timothy (*Phleum pratense*)), and four soils with differing texture, organic carbon content, and cation exchange capacity. The endpoints measured were emergence, biomass, root length, and shoot length (Table 2.4).

For all four plant species, the most sensitive endpoint was root length elongation, with the lowest LOECs ranging from 440 mg kg^{-1} (alfalfa in till) to 940 mg kg^{-1} (lettuce emergence, lettuce root length, and carrot root length in till). The highest LOEC was >23,700 mg kg^{-1} for alfalfa shoot length in loam. Plants were generally most sensitive to sulfolane in till and least sensitive in loam (Table 2.4).

2.8 Behavior and Effects in Aquatic Biota

Available data on the toxicity of sulfolane to freshwater and marine aquatic species are presented in Table 2.5. The majority of the data were for freshwater species. However, for completeness, marine data were also included in Table 2.5 in case they are required at a future date. Data gaps in the marine dataset are noted in Section 3.6.2.

Toxicological studies on rainbow trout (*Oncorhynchus mykiss*) and the sideswimmer (*Hyalella azteca*) were commissioned for CAPP (2001). A full report on this work is included in CAPP (2001). In addition, Environment Canada (2003) commissioned a toxicological study on the daphnid (*Daphnia magna*). Note that ERAC (1998) included a review of previous published and unpublished freshwater aquatic toxicological data, and a report on freshwater toxicological studies which were commissioned for the ERAC (1998) report. References to ERAC (1998) in

the following sections refer only to the new data commissioned for the report. Original references are used for other studies referenced in the ERAC (1998) report.

2.8.1 Freshwater Aquatic Life

2.8.1.1 Aquatic Vertebrates

Data were available for five species of aquatic vertebrates (Table 2.5). An acute lethality study on rainbow trout (*Oncorhynchus mykiss*) was completed for CAPP (2001). ERAC (1998) completed a 7 day survival and growth test on fathead minnows (*Pimephales promelas*). The results of acute lethality studies on goldfish (*Carassius auratus*), mosquito fish (*Gambusia sp.*), and stickleback (species not specified) were also available. Reported LC_{50} values for the acute tests ranged from 1,264 mg L^{-1} (rainbow trout) to 4,800 mg L^{-1} (goldfish). No adverse effect was observed on survival or growth of the fathead minnow at 1,000 mg L^{-1} (the highest concentration used in the test).

2.8.1.2 Aquatic Invertebrates

Seven studies considered the toxicity of sulfolane to three species of aquatic invertebrates (Table 2.5). An acute lethality study on a sideswimmer (*Hyalella azteca*) was completed for CAPP (2001). Four studies reported the acute lethality of sulfolane to *Daphnia magna*, and two studies investigated the 7 day reproduction and survival endpoints in *Ceriodaphnia dubia*. Reported LC_{50} values for the acute tests ranged from 40 mg L^{-1} (*D. magna*) to 3,274 mg L^{-1} (also for *D. magna*). Details of the test protocols for all three *D. magna* studies were available, but provided no insight into why the reported LC_{50} values should vary by almost two orders of magnitude. The LOECs for the non-lethal (reproduction) endpoint for *C. dubia*, ranged from 375 mg L^{-1} to 500 mg L^{-1}.

2.8.1.3 Aquatic Plants

Only one study for an aquatic vascular plant was available. SRC (1994) reported the EC_{50} for duckweed (*Lemna minor*) growth to be >2,500 mg L^{-1}. Three studies on the green alga *Selenastrum capricornutum* were available for various non-lethal endpoints. The lowest EC_{50} value was 723 mg L^{-1} from the ERAC 1998 growth endpoint study. Other studies and other endpoints all gave EC_{50} values greater than 1,000 mg L^{-1}.

2.8.1.4 Other Aquatic Biota

Other aquatic biota include all aquatic organisms not included in the animal or plant kingdoms. This covers organisms from the kingdoms Monera, Protista, and Fungi. A study by SRC (1994) measured ^{14}C uptake and nitrogen fixation by the cyanobacteria *Aphanizomenon flos-aquae* and

^{14}C uptake by the diatom *Cyclotella meneghiana*. The EC_{50} values reported were all greater than or equal to 500 mg L^{-1}.

2.8.2 Marine Life

2.8.2.1 Marine Vertebrates

Literature data were not available for marine vertebrates

2.8.2.2 Marine Invertebrates

Three studies considered the toxicity of sulfolane to marine invertebrates. Acute lethality studies using the copepod *Acartia tonsa* (Girling, 1987) and the oyster *Crassostrea gigas* (Fairhurst *et al.*, 1992) yielded LC_{50} values ranging from 52 mg L^{-1} (48 hour duration) to 460 mg L^{-1} (24 hour duration). A NOEC of 150 mg L^{-1} was obtained for the non-lethal (growth) endpoint of the mysid shrimp *Mysidopsis bahia* during a 7 day, chronic study (Wong *et al.*, 1993).

2.8.2.3 Marine Plants

Literature data were not available for marine plants.

2.8.2.4 Other Marine Biota

Other marine biota include all marine organisms not included in the animal or plant kingdoms. This covers organisms from the kingdoms Monera, Protista, and Fungi. Two studies examined the effect of sulfolane on the luminescence of the marine bacterium *Vibrio fischerii* (SRC, 1994; ERAC, 1998). Reported EC_{50} values ranged from 30 to 59 mg L^{-1}.

2.9 Behavior and Effects in Mammalian Species and Humans

2.9.1 Mammalian Species

Available studies on the mammalian toxicology of sulfolane up to May 2000 were reviewed by Cantox. The complete Cantox report is available in CAPP (2001). As a result of data gaps identified in this review, a subchronic (13 week) oral rat study was commissioned. This study was conducted at Huntingdon Life Sciences (HLS, 2001). This section represents a summary of the Cantox report in combination with a summary of HLS (2001). Acute studies on mammals are summarized in Table 2.6.

2.9.1.1 Acute Toxicity Studies

There was minimal evidence of acute toxicity from sulfolane administered by various routes in rats, mice, guinea pigs, and rabbits. Studies by Andersen *et al.* (1976) indicated little variation between the LD_{50} of oral, parenteral, and subcutaneous administered doses, while the intravenous LD_{50} was approximately half that seen by the other routes of exposure. Regardless of the route of administration or species, sulfolane produced toxic signs indicative of central nervous system (CNS) stimulation or depression (dependent on dose).

Inhalation Studies

Sulfolane has a low vapour pressure (Table 2.2), therefore, exposure via inhalation is unlikely at normal temperatures. Saturated vapours or mist suspensions can produce headache, nausea, vomiting, and decrease white blood cells (leukopenia). Neurological evidence of a response to inhaled sulfolane mists includes tremors and seizures. The effects observed in these exposures will be reviewed below under subchronic toxicity studies.

Oral Studies

In acute toxicity studies by Andersen *et al.* (1976), oral LD_{50} estimates for guinea pigs and rats were determined as 1,815 and 1,846 mg sulfolane kg^{-1} bodyweight, respectively (Table 2.6). Administration of sulfolane produced hyperactivity, followed by clonic-toxic convulsions.

Brown *et al.* (1966) reported a single dose, acute, oral LD_{50} of 2,100 mg kg^{-1} bw in exposed guinea pigs (Table 2.6). All animals that died, did so within 24 hours and typically in less than 3 hours. In each case, death was preceded by convulsions and gasping for breath. Similar tests on mice led to death within 24 hours (letter from Exxon Biomedical Sciences, 1986).

Zhu *et al.* (1988) reported on the toxicokinetics of orally administered ^{3}H-sulfolane to the rat in a study that investigated the maximum allowable concentration of sulfolane in surface water. Acute oral LD_{50}'s in white rats, mice, and guinea pigs were determined as 2,504, 2,343, and 1,445 mg kg^{-1} bw, respectively (Zhu *et al.*, 1987; Table 2.6). The authors indicate similar symptoms were immediately evident in each of the three test animals. The test subjects became more active, short of breath, and demonstrated rigid tails, twitching, rear leg shaking, and stiffening a few minutes following administration.

Percutaneous and Intraveneous Administration

Andersen *et al.* (1976) reported parenteral LD_{50}'s ranging from 1,270 to 1,598 mg kg^{-1} bw in rats, mice, and guinea pigs, and intravenous LD_{50}'s ranging from 632 to 1,094 mg kg^{-1} bw for rats, mice, and rabbits exposed to sulfolane. Oral, parenteral, and intravenous exposures approaching, or in excess of the LD_{50}, resulted in toxic signs indicative of CNS stimulation.

Gordon *et al.* (1984) noted that a parenteral injection of approximately half the LD_{50} (799 mg kg^{-1} bw) resulted in a depressed metabolic rate and hypothermia in rats, which lasted at least 2.5 hours. The authors speculated sulfolane toxicity may be partially due to its effects on body temperature (*i.e.*, depression of thermoregulation). Similar results were observed in studies by Ruppert and Dyer (1985).

Subcutaneous injections of 9, 100, 200, 400, 600, and 750 mg of sulfolane kg^{-1} bw at an ambient temperature of 10° C caused a dose-dependent decrease in the colonic temperature of rabbits (Mohler and Gordon, 1988). The observed thermoregulatory response to sulfolane appeared to be a function of the ambient temperature.

Dermal and Ocular Studies

Dermal application of sulfolane resulted in no apparent skin irritation or damage in test rabbits (Brown *et al.*, 1966). Furthermore, sulfolane did not produce signs of sensitization in either topical or intradermal tests. Undiluted sulfolane (0.2 ml) instilled into the right eyes of rabbits produced only a mild conjunctivitis, which cleared within a few hours.

2.9.1.2 Subchronic and Chronic Toxicity Studies

Three studies were available in this category. These studies are reviewed below.

Andersen* et al. *(1977)

Andersen *et al.* (1977) conducted subchronic (90 day) inhalation toxicity studies with rats, guinea pigs, beagle dogs, and squirrel monkeys. Animals were routinely evaluated for signs of potential toxic effects, such as alterations in physical appearance, locomotor activity, breathing patterns, appetite, or behaviour. Animals were also weighed and bled for hematological testing after 30 and 60 exposure-days, and at the end of the study. Blood, major organs, and tissues were also collected from each animal at the end of the study. Urinalysis examined pH, protein, sugar, ketone bodies, and occult blood at 24 hour intervals collected from the rats and guinea pigs. Six subchronic exposure studies were conducted: one study involved repeated exposure to 495 mg m^{-3} for 8 hr day^{-1}, 5 days $week^{-1}$ for 27 exposure days, and five studies looked at 23 hr day^{-1}, continuous exposures of approximately 90 day duration to 200, 159, 20, 4.0, and 2.8 mg m^{-3}.

Inhalation of atmospheres containing high concentrations (3,600 and 4,700 mg m^{-3}) of aerosolized sulfolane resulted in leukopenia and convulsions within 24 hours. Concentrations of 200 and 495 mg sulfolane m^{-3} resulted in convulsions, vomiting, and death in exposed squirrel monkeys, while dogs convulsed, vomited, and were unusually aggressive during continuous

exposure to 200 mg m^{-3}, but not during repeated exposures to 495 mg m^{-3}. While deaths of two squirrel monkeys were seen at the 200 mg m^{-3} exposure level (on days 3 and 4), both monkeys were heavily infested with parasites, potentially playing a role in their susceptibility to sulfolane toxicity. While none of the rodents convulsed at any of the subchronic exposures, histological investigations indicated leukopenia and increased plasma transaminase activity in guinea pigs exposed to 200 mg m^{-3}, but not those exposed to 159 mg m^{-3}.

None of the toxic effects observed at 200 mg m^{-3} in any of the test species were found on exposure to concentrations of 20 mg m^{-3} or lower. As such, the exposure concentration of 20 mg m^{-3} could be considered the no-observable-adverse-effect-level (NOAEL).

Zhu* et al. *(1987)

A study of the chronic toxicity of sulfolane administered orally to guinea pigs (which had just stopped breast-feeding) at dose levels of 0.25, 2.5, 25, and 250 mg kg^{-1} bw was reported by Zhu *et al.* (1987). Forty guinea pigs, with equal numbers of males and females, were exposed to sulfolane for six months in each of the dose groups, and one control group. Biochemical and pathological evaluations were conducted on a subset of each dose group following three months of exposure, with minor effects observed in the 2.5, 25, and 250 mg kg^{-1} bw dose groups. Pathological tissue inspection indicated the main pathological change involved shrinkage of white pulp in the spleen.

After six months of exposure, significant changes were observed in a number of liver biochemical indices for the 250 mg kg^{-1} bw male guinea pig group, with some changes noted in the 25 mg kg^{-1} bw group. Pathological examinations indicated a significant increase in fatty deposits in the liver tissue for the 2.5, 25, and 250 mg kg^{-1} bw exposure groups. Shrinkage of spleen white pulp and decreasing cell counts in spinal marrow were also noted in these three dose groups. No biochemical or pathological changes were found in the 0.25 mg kg^{-1} bw dosage group.

Based on these study results, the authors reported a chronic threshold and no-effect doses for sulfolane of 2.5 and 0.25 mg kg^{-1} bw bodyweight, respectively, and a maximum allowable concentration (MAC) of 5 mg L^{-1} in drinking water for humans (Zhu *et al.*, 1987).

Huntingdon Life Sciences (2001)

The Huntingdon Life Sciences (HLS, 2001) study involved exposure of rats to sulfolane in their drinking water for 13 weeks at concentrations of 0, 25, 100, 400, and 1,600 mg L^{-1}, which was calculated by HLS to be equivalent to the following levels:

Males: 2.1, 8.8, 35, and 131.7 mg kg^{-1} bw day^{-1}

Females: 2.9, 10.6, 42, and 191.1 mg kg^{-1} bw day^{-1}

The sulfolane exposure was reported to be well tolerated, with the only adverse effects being a nephropathy in male rats at the two highest doses, and reduced white blood cell (WBC) counts in females in the three highest dose groups.

The nephropathy is typical of the well-known phenomenon specific to male rats that occurs following prolonged exposure to many hydrocarbons and derivatives, and is not considered to be of toxicological relevance to humans. The stated NOAEL for male rats in this study, with nephropathy as the endpoint, was 8.8 mg kg^{-1} day (100 mg sulfolane L^{-1} drinking water).

The WBC reductions are consistent with observations from the Andersen *et al.* (1977) inhalation study. In the latter investigation they occurred after a single, high concentration, 17.5 hour exposure, as well as after longer term exposures at the higher test concentrations in both sexes of rat (no data is given for female rats in the Andersen *et al.* (1977) paper, but male rats were definitely susceptible, whereas they were unaffected in the HLS (2001) study). WBC reductions were also observed in squirrel monkeys and guinea pigs exposed to high doses, but not in any of the four tested species after prolonged inhalation of 20 mg m^{-3}. A WBC reduction after a single exposure, as occurred in the Andersen *et al.* (1977) study, indicates a direct toxic effect on the WBCs. No pathological lesions were found in the females. The NOAEL in female rats in the HLS (2001) study was 2.9 mg kg^{-1} bw day^{-1} (25 mg sulfolane L^{-1} drinking water).

2.9.1.3 Genetic Toxicology Studies

When evaluating data for genotoxicity, primary goals are to determine (1) the likelihood of occurrence of a key event and (2) whether that event might lead to heritable changes associated with any adverse effect *in vivo*, including cancer. The basis upon which a weight-of-evidence evaluation can be constructed includes the following:

- Any statistically significant observations should be reproducible and biologically significant;
- A dose-response relationship should exist for effects;
- The effects should be permanent and progressive, as opposed to reversing upon cessation of chemical dosing;
- The nature of DNA effects should be characterized;
- The database should be consistent or inconsistencies adequately explained; and,
- The effects produced in the assay should be relevant to humans.

A central objective of the weight-of-evidence approach is to balance experimental test data with experience, and not to accord greater weight to any single result. For purposes of human hazard assessment, greater confidence is placed in those test systems that examine possible genetic

effects from chemical exposure of animals, rather than in tests that rely on selected homogeneous cell populations raised and tested *in vitro*. Chemical exposures of biological systems carried out *in vitro* are much less realistic, and results of such tests can be determined by the effects of toxicity. Such toxicity can occur at unusually high exposure concentrations and/or be dependent on metabolic and detoxification capabilities. Finally, a weight-of-evidence evaluation seeks to establish a dose-response relationship. Greater attention should be given wherever there is a clear association between increased exposure and a genetic effect.

Sulfolane has never been assessed by mammalian cancer bioassays. The structurally related compound, 3-sulfolene was assessed by the National Cancer Institute and was found to be negative in a gavage carcinogenicity study in Osborne-Mendel rats and B6C3F1 mice (NCI, 1978).

The bacterial mutagenic activity of sulfolane was investigated in *Salmonella typhimurium* (strains TA1525, TA1537, TA1538, TA98, and TA100) and *Escherichia coli* (WP_2 and WP_2-*uvr A*) tester strains. Eucaryotic mutagenic activity was also examined in the yeast *Saccharomyces cerevisiae* (JD 1). These assays were conducted either in the presence or absence of an S9 microsomal fraction obtained from a liver homogenate from rats pretreated with Aroclor. At concentrations up to 4,000 µg per plate, sulfolane was not mutagenic to *E. coli* or *Salmonella* either in the presence or absence of a rat liver S9. Results in the *Saccharomyces* mitotic gene conversion assay with or without S9 also indicated sulfolane was non-mutagenic/genotoxic at concentrations up to 5 mg ml^{-1} (Shell, 1982). Similar assays on five *Salmonella typhimurium* strains (TA1535, TA1537, TA1538, TA98, and TA100) were also tested by Phillips (1984). Exposure to five graded doses of sulfolane in the presence of and in the absence of metabolic activation did not increase reversion rates of histidine prototrophy.

Phillips (1984) conducted an *in vitro* sister chromatid exchange (SCE) assay using Chinese hamster ovary cells and a minimum of five doses of sulfolane, with and without metabolic activation by an Aroclor-induced rat liver microsomal fraction. A statistically significant increase in the number of SCE per chromosome was observed only at the highest dose (6.4 mg ml^{-1}) in the absence of metabolic activation. There were no significant increases observed at the remaining doses, so there was no evidence of a dose-response. Since only one dose of sulfolane exhibited a statistically significant increase in SCEs, but no dose produced an overall two-fold increase in SCE's, it was concluded the criteria for a positive test were not met. Therefore sulfolane was considered negative for the production of SCE *in vitro* (Phillips, 1984).

In primary cell cultures of rat liver RL-4 cells, sulfolane at doses of 0.1, 0.25, and 1.0 mg ml^{-1} *in vitro* was negative in a chromosomal aberration test (Shell, 1982).

In the mouse lymphoma forward mutation assay performed in the L5178Y TK+/- a minimum of eight doses of sulfolane were tested with and without metabolic activation by an Aroclor-induced rat liver microsomal fraction. Sulfolane treatment resulted in an increased induction of forward mutations at the TK locus for some doses, but failed to exhibit a dose-response relationship. Under the accepted criteria for the test, it was concluded that sulfolane was mutagenic in this assay (Phillips, 1984).

In the various mutagenicity and genotoxicity assays, sulfolane was not mutagenic in bacteria or yeast, and showed no evidence of being capable of producing structural alterations *in vitro* such as chromosomal aberrations in primary rat liver cultures, or SCE (Chinese hamster ovary cells). On the other hand, there is one report of a positive response at the highest dose in the mouse lymphoma assay, but no clear dose-response. Based on the criteria described, there is insufficient evidence to conclude that sulfolane is genotoxic, and the single mouse lymphoma assay response may suggest cytotoxicity at extremely high doses. A quantitative structure-activity relationship study on some sulfolanes has suggested that they may perform an activity as human immunodeficiency virus-1 (HIV-1) protease inhibitors (Gupta *et al.*, 1998). It is possible that protease inhibition could be responsible for the increase in responses for chemical exposure such as SCE, and possibly mutations at very high exposures. In any case, one positive test should not be given greater weight than the four or five negative responses observed with sulfolane.

2.9.1.4 Reproduction and Developmental Studies

No reliable long-term reproductive or developmental studies have been conducted on sulfolane. However, limited information is available in (Zhu *et al.*, 1987) concerning possible teratogenic effects in rats (fetus absorption and fetus skeleton abnormality) at very high doses of sulfolane.

2.9.1.5 Absorption, Biotransformation, and Excretion

Research has indicated that sulfolane is rapidly and readily absorbed from the oral and inhalation routes, but poorly absorbed from the dermal route of administration (Andersen *et al.*, 1976; Ursin *et al.*, 1995). Andersen *et al.* (1976) conducted a number of absorption and metabolism studies in various species (*i.e.*, rats, guinea pigs, rabbits, and mice). Following an intraperitoneal administration of 100 mg of ^{35}S-sulfolane kg^{-1}, 85% of the radioactivity excreted in the urine during the first 24 hours was associated not with sulfolane itself, but with a metabolite, identified as 3-hydroxysulfolane (Andersen *et al.*, 1976). Further excretion studies indicated that at low doses much of the sulfolane was excreted in its metabolized form in the urine and, with increasing dose, a larger proportion of the dose was excreted as unmetabolized sulfolane. These data indicate the presence of a saturable metabolic system.

Based upon blood-sulfolane decay curves obtained following intravenous injections of sulfolane, Andersen *et al.* (1976) estimated sulfolane was rapidly distributed throughout the body and then slowly removed from plasma with a half-life of 3.5 to 5 hours.

While route-specific bioavailability estimates cannot be predicted based upon an intraperitoneal administration, given 85% of the sulfolane was excreted in a metabolized form, one would expect an internalized dose to be highly bioavailable.

2.9.2 Humans

2.9.2.1 Acute Toxicity Studies

Acute inhalation, oral, percutaneous administration, intravenous administration, dermal, and ocular studies on humans were not available in toxicity literature for sulfolane.

2.9.2.2 Subchronic and Chronic Toxicity Studies

Subchronic studies on humans were not available in toxicity literature for sulfolane.

2.9.2.3 Genetic Toxicology Studies

Genetic toxicology studies on humans were not available in toxicity literature for sulfolane.

2.9.2.4 Reproduction and Developmental Studies

Reproduction and developmental studies on humans were not available in toxicity literature for sulfolane.

2.9.2.5 Absorption, Biotransformation, and Excretion

Absorption, biotransformation, and excretion studies on humans were not available in toxicity literature for sulfolane.

3. DERIVATION OF ENVIRONMENTAL AND HUMAN HEALTH SOIL AND WATER QUALITY GUIDELINES

3.1 Freshwater Aquatic Life

Freshwater aquatic life guidelines for sulfolane were developed using the Protocol ("*A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life*"; CCME,

1999). The following sections summarize the requirements of the Protocol and discuss the available dataset in terms of these requirements. The toxicological dataset was summarized in Table 2.5, and discussed in Section 2.8.

The Protocol defines (1) the requirements for a toxicological study to be acceptable for guideline derivation (data quality requirement), (2) the minimum required dataset for Full and Interim guideline development (data quantity requirement), and (3) the process for deriving guidelines. The following paragraphs provide a summary of the requirements of the Protocol, and assess the toxicological dataset.

3.1.1 Data Quality

The data quality requirement in the Protocol may be summarized as follows. For a toxicological study to be considered "Secondary Data", all relevant environmental variables (*e.g.*, temperature, pH, hardness, dissolved oxygen, etc.) should be measured and reported, and the survival of controls must be reported. For data to be considered "Primary Data", tests must employ currently acceptable practices, concentrations must be measured at the beginning and end of a test, and, in general, dynamic (*i.e.*, flow-through) tests are required. Data that do not conform to the requirements for Primary or Secondary Data are "Unacceptable Data".

The toxicological dataset is summarized in Table 2.5 and classified as primary, secondary, or unacceptable. Only the CAPP (2001) data conformed to all the requirements for Primary Data. Studies by ERAC (1998) and Girling (1987) were classified as Secondary Data. All other studies were classified as Unacceptable Data. It should be noted that studies classified as "Unacceptable Data" may, in fact, represent acceptable (*i.e.*, Primary or Secondary) data, but insufficient information was available to confirm this. According to the Protocol only Primary or Secondary Data can be used in the guideline derivation process.

3.1.2 Data Quantity

The Protocol requirement for the quantity of Primary and/or Secondary data for Interim freshwater aquatic life guidelines may be summarized as follows. At least two studies on freshwater fish species, and at least two studies on freshwater invertebrate species are required. The tests may be acute or chronic. One of the fish must be a cold water species, and two different classes of invertebrates must be represented, one of which includes a planktonic species resident in North America (*e.g.*, daphnid).

The Protocol requirements were met by the Primary and Secondary Data in Table 2.5. The acute tests on rainbow trout and fathead minnow fulfill the requirement for tests of two freshwater fish species, with the rainbow trout fulfilling the requirement for a cold water species. Acceptable

test results are available for three species of invertebrate: *Daphnia magna* and *Ceriodaphnia dubia*, representing the Class Branchiopoda and *Hyalella azteca*, representing the Class Malacostraca.

Thus all the Protocol requirements for data quantity are met.

3.1.3 Guideline Derivation

"Guidelines are preferably derived from the lowest-observable-effect-level (LOEL) from a chronic study using a non-lethal endpoint for the most sensitive life stage of the most sensitive aquatic species investigated. The most sensitive LOEL is multiplied by a safety factor of 0.1 to arrive at the guideline value" (CCME, 1999). The lowest chronic LOEC for Primary or Secondary Data in this dataset is 500 mg L^{-1} for the 7 day reproduction endpoint for *Ceriodaphnia dubia*. This yields a guideline value of 50 mg L^{-1}.

3.2 Marine Aquatic Life

A marine life guideline for sulfolane could not be developed using the Protocol ("A *Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life*; CCME, 1999) due to insufficient data quality and data quantity. The following sections summarize the requirements of the Protocol and discuss the available dataset in terms of these requirements. The toxicological dataset was summarized in Table 2.5, and discussed in Section 2.8.

The Protocol defines (1) the requirements for a toxicological study to be acceptable for guideline derivation (data quality requirement), (2) the minimum required dataset for Full and Interim guideline development (data quantity requirement), and (3) the process for deriving guidelines. The following paragraphs provide a summary of the requirements of the Protocol, and assess the toxicological dataset.

3.2.1 Data Quality

The data quality requirement in the Protocol may be summarized as follows. For a toxicological study to be considered "Secondary Data", all relevant environmental variables (*e.g.*, temperature, pH, hardness, dissolved oxygen, etc.) should be measured and reported, and the survival of controls must be reported. In addition, for data to be considered "Primary Data", tests must employ currently acceptable practices, concentrations must be measured at the beginning and end of a test, and, in general, dynamic (*i.e.*, flow-through) tests are required. Data that do not conform to the requirements for Primary or Secondary Data are "Unacceptable Data".

The toxicological dataset is summarized in Table 2.5. A study by Girling (1987) on the copepod *Acartia tonsa* was classified as secondary and the four other studies on marine organisms were classified as unacceptable. It should be noted that studies classified as "Unacceptable Data" may, in fact, represent acceptable (*i.e.*, Primary or Secondary) data, but insufficient information was available to confirm this. According to the Protocol only Primary or Secondary Data can be used in the guideline derivation process.

3.2.2 Data Quantity

Since no primary studies and only one secondary study on marine life was available in the toxicological literature, the marine life guideline could not be developed. The Protocol requirement for the quantity of Primary and/or Secondary Data for Interim marine life guidelines may be summarized as follows. At least two studies on marine fish species, and at least two studies on marine invertebrate species are required. The tests may be acute or chronic. One of the fish must be a temperate species, and two different classes of invertebrates must be represented.

The Protocol data quantity requirements were not met by the data in Table 2.5.

3.2.3 Guideline Derivation

A marine life guideline for sulfolane could not be developed using the Protocol due to insufficient data quality and data quantity.

3.3 Irrigation

Irrigation water quality guidelines for sulfolane were developed using the Protocol ("*Protocols for Deriving Water Quality Guidelines for the Protection of Agricultural Water Uses*"; CCME, 1999). The toxicological data set was sufficient to derive Interim guidelines (Table 2.4). Data in Table 2.4 are classified as primary toxicological data by the Protocol. As laid out in the Protocol, irrigation guidelines were calculated for (1) tame hay, cereals, and pasture crops (*e.g.*, alfalfa and timothy) and (2) other crops (*e.g.*, lettuce and carrot).

As can be seen in Table 2.4, the sensitivity of plants to sulfolane varies strongly depending on soil type. For most plant species and endpoints, plants were most sensitive to sulfolane in sand or till, and least sensitive in loam. Accordingly, guidelines were calculated for "poor soil" (*i.e.*, sand or till), and loam. The reason for this approach was to provide both an overall irrigation guideline, which was protective of crop growth on any soil type, and guidance on tolerable levels of sulfolane when crops are being grown on typical, improved, agricultural soils.

Four guidelines are presented in Table 3.1, for each of the two soil types (poor soil and loam) and two crop types (tame hay, cereals, and pasture crops and other crops) noted above. The overall irrigation guideline is the lowest of these four guidelines. The detailed guideline derivation process is described below.

The first step in the guideline derivation process was the calculation of the acceptable soil concentration (ASC), which is an estimate of the soil concentration that would not result in adverse effects on crops over the course of one growing season:

$$ASC\ (mg\ kg^{-1}) = \left(\frac{\sqrt{LOEC \times NOEC}}{UF} \right)$$

Where: LOEC = lowest-observed-effect-concentration (mg kg^{-1} soil);
NOEC = no-observed-effect-concentration (mg kg^{-1} soil); and,
UF = uncertainty factor of 10 (as per the Protocol).

The lowest calculated ASCs for each crop group and soil type were as follows:

- 58 mg kg^{-1} - cereals, tame hays, and pasture crops grown in loam, based on the biomass endpoint for timothy;
- 26 mg kg^{-1} - cereals, tame hays, and pasture crops grown in poor soil, based on the root length endpoint for alfalfa in till;
- 233 mg kg^{-1} - other crops grown in loam, based on the root length endpoint for lettuce and carrot; and,
- 51 mg kg^{-1} - other crops grown in poor soil, based on the root length endpoint for lettuce in till.

The next step in the guideline derivation process was to calculate species maximum acceptable toxicant concentration (SMATC), which is the maximum amount of contaminant allowed in a 1 ha (100 m x 100 m) plot. The SMATC was calculated as:

$$SMATC\ (mg\ L^{-1}) = \left(\frac{ASC \times \rho \times L \times W \times D}{IR} \right)$$

Where: ASC = acceptable soil concentration (mg kg^{-1});
ρ = soil bulk density (1,300 kg m^{-3});
L = length (100 m);
W = width (100 m);

D = depth (0.15 m for other crops and 0.5 m for tame hays, cereals, pasture crops); and,
IR = irrigation rate per year (1.2×10^7 L ha^{-1}).

The SMATC for cereals, tame hays, and pasture crops was 95 mg L^{-1} (loam), and 42 mg L^{-1} (poor soil). For other crops it was 38 mg L^{-1} (loam), and 8.4 mg L^{-1} (poor soil). These values are proposed as Interim irrigation water quality guidelines (Table 3.1).

3.4 Livestock Watering

Livestock watering guidelines for sulfolane were developed using the Protocol ("*Protocols for Deriving Water Quality Guidelines for the Protection of Agricultural Water Uses*", CCME, 1999).

The Protocol defines (1) the requirements for a toxicological study to be acceptable for guideline derivation (data quality requirement), (2) the minimum required dataset for Full and Interim guideline development (data quantity requirement), and (3) the process for deriving guidelines. The following sections summarize the requirements of the Protocol and discuss the available dataset in terms of these requirements. The toxicological dataset is summarized in Table 2.6, and discussed in Section 2.9.

3.4.1 Data Quality

The data quality requirement in the Protocol may be summarized as follows. For a toxicological study to be considered "Secondary Data", the dose, duration of exposure and effects should be reported, the response and survival of controls must be reported. Secondary Data may be for any route of exposure (*e.g.*, oral, inhalation, dermal). Secondary Data does not have to conform to accepted laboratory practices as long as all necessary information is reported. For data to be considered "Primary Data", tests must employ currently acceptable laboratory practices, report dose in standard units (*i.e.*, mg kg^{-1} bw day^{-1} for chronic tests and mg kg^{-1} bw for acute tests), report the response and survival of controls, and report the scientifically valid statistics used. In addition, it is preferred that Primary Data (1) have doses measured analytically, (2) be through a simulated drinking water exposure (*e.g.*, *ad libitum*, gavage, oesophageal cannula, or rumen fistula of food and water), (3) be full life cycle studies, and (4) examine sensitive endpoints (*e.g.*, development, growth, fecundity) and production parameters (*e.g.*, milk yield, litter size, feed conversion). Data that do not conform to the requirements for Primary or Secondary Data are "Unacceptable Data".

3.4.2 Data Quantity

The minimum toxicological dataset required by the Protocol for derivation of Interim guidelines is two acute or chronic studies on two or more mammalian species raised in Canada including at least one livestock species, and at least one acute or chronic study on one or more avian livestock species. The minimum dataset requirements were not therefore met, but in spite of this, it was felt that it would be useful to calculate a Preliminary livestock watering guideline based on the available data.

Procedures exist in the Protocol for calculating a livestock watering guideline from either acute or chronic toxicological data. Available mammalian toxicological data for sulfolane were reviewed and discussed in Section 2.9. The acute studies by Zhu *et al.* (1987), Andersen *et al.* (1976) and Brown *et al.* (1966) were chosen for derivation of a Preliminary guideline for livestock watering for the following reasons:

- the data set (Table 2.6) includes 16 data points from three studies, using four species (rat, mouse, guinea pig, and rabbit) and four routes of administration (oral, intraperitoneal, intravenous, and subcutaneous);
- good agreement is seen between data for four different species from two mammalian orders (rodents and lagomorphs), providing some confidence in making an extrapolation to livestock species;
- good agreement is seen between data for four routes of administration;
- good agreement is seen between data from three different studies; and,
- overall, the data are very consistent.

The acute dataset exhibits a mean LD_{50} of 1,540 mg kg^{-1} bw, and a standard deviation of 550 mg kg^{-1} bw.

3.4.3 Guideline Derivation

The first step in the guideline derivation process laid down in the Protocol for acute data was the calculation of the TDI, which was based on an extrapolation of acute to chronic data (CCME, 1999):

$$TDI\ (mg\ kg^{-1}\ bw\ day^{-1}) = \left(\frac{LD_{50}}{70 \times UF} \right)$$

Where: LD_{50} = lethal dose to 50% of the population (1,540 mg kg^{-1} bw day^{-1}; Table 2.6);
70 = extrapolation factor from acute to chronic data (CCME, 1999); and,

UF = uncertainty factor (10; CCME, 1999).

Based on the acute to chronic extrapolation, the TDI for sulfolane applicable to livestock is 2.2 mg kg^{-1} bw day^{-1}.

The next step in the guideline derivation process was to calculate the reference concentration (RC), which represents the livestock watering guideline. The reference concentration is calculated using the body weight and water ingestion rate of particular species. Dairy cattle and beef cattle were selected to represent livestock; deer were also considered to help assess possible risks to other species. The equation used was:

$$RC \cdot (mg\ L^{-1}) = \left(\frac{TDI \times BW}{WIR} \right)$$

Where: TDI = tolerable daily intake (2.2 mg kg^{-1} day^{-1}; calculated above);
BW = body weight (862 for dairy cattle (CCME, 1999), 730 kg for beef cattle (CCME, 1999), and 68 kg for deer (Smith, 1993); and,
WIR = daily water intake rate (137 L day^{-1} for dairy cattle, CCME (1999), data for lactating cows at 21° C), 80 L day^{-1} for beef cattle (CCME, 1999), and 4.4 L day^{-1} for deer (Smith, 1993).

The RCs for dairy cattle, beef cattle, and deer were 14, 20, and 34 mg L^{-1}, respectively. These values are recommended as Preliminary livestock watering guidelines (Table 3.1).

3.5 Source Water for Drinking

The generic scenario assumed to develop source water for drinking guidelines was the "Agricultural Land Use" scenario defined by the Protocol. This scenario assumes a farm with a family including children resident on the property who use groundwater for drinking water. Guidelines are calculated for an adult and a child. The most sensitive human receptor would be a child.

Humans could be exposed to sulfolane in groundwater by (1) ingestion of drinking water and water used to cook and (2) dermal contact during bathing and washing. While individuals could be exposed to sulfolane in surface water via swimming and/or fishing, this exposure pathway will be minimal relative to those noted above. A dermal contact check is provided to evaluate the relative importance of this exposure pathway.

3.5.1 Tolerable Daily Intake (TDI)

The Tolerable Daily Intake (TDI) is defined as the intake to which it is believed a receptor can be exposed over a lifetime without deleterious effects. The TDI represents the combination of: 1) real values for toxicological endpoints when no evidence of adverse effects can be detected in experimental animals or humans (*i.e.*, the no-observable-adverse-effect level, or NOAEL); and, 2) safety factors that account for possible differences between responses in the species tested and humans, sensitivity of human populations, and other factors that contribute to the uncertainty of lack of observed effects in experimental conditions. The introduction of safety factors is a concept that has had wide acceptance in the scientific and regulatory communities around the world.

The TDI is calculated as (see also CAPP (2001)):

$$TDI = \left(\frac{NOAEL}{Safety\ Factor} \right)$$

3.5.1.1 Selection of Study

Three following chronic or subchronic studies for sulfolane were reviewed in Section 2.9.1.2:

- Andersen *et al.* (1977);
- Zhu *et al.* (1987); and,
- Huntingdon Life Sciences (HLS, 2001).

The human TDI was based on the HLS (2001) study. This study was preferred over the Andersen *et al.* (1977) study due to a more applicable route of administration (oral versus inhalation). Zhu *et al.* (1987) was not used to develop a human TDI due to uncertainties in the interpretation of some of the toxicological endpoints and the lack of data available to confirm that "good laboratory practice" GLP had been followed in this study.

The NOAEL for female rats in the HLS (2001) study was 2.9 mg kg^{-1} bw day^{-1} (25 mg L^{-1} sulfolane L^{-1} drinking water).

3.5.1.2 Selection of Safety Factors

The Joint European Committee on Food Additives (JECFA) proposed principles for determining a margin of safety, and has developed a methodology to establish an acceptable value for a factor that would directly link animal toxicological data to human health and safety (FAO/WHO, 1958). The margin of safety allows for any species differences in susceptibility, the numerical

differences between the test animals and the exposed human population, the greater variety of complicating disease processes in the human population, the difficulty of estimating the human intake, and the possibility of synergistic action. JECFA stated that the 100-fold margin of safety applied to the maximum ineffective dosage (expressed in mg kg^{-1} body weight day^{-1}) was believed to be an adequate factor (FAO/WHO, 1958). The value of 100 has been regarded as comprising two factors of ten to allow for interspecies and intraspecies variation (WHO, 1994).

The validity and size of safety/uncertainty factors, and their application across many substances including pesticides has undergone periodic re-evaluation (Renwick and Lazarus, 1998). By and large, the allocation of appropriate safety factors is considered on a case-by-case basis, relying on analysis of the total weight of evidence including a consideration of data gaps (WHO, 1990). WHO Scientific Groups have confirmed a 100-fold safety factor as an adequate and useful guide, particularly when there are few toxicological data gaps (WHO, 1967; 1994).

The National Research Council report on Pesticides in the Diets of Infants and Children (NRC, 1993) indicated the current 10-fold intraspecies factor adequately protects for socioeconomic, nutritional, and health status factors that influence the vulnerability of children to environmental toxicants.

Based on the review presented above, two 10-fold safety factors to allow for interspecies and intraspecies variation were considered appropriate for sulfolane. In addition, a three-fold safety factor was applied to account for all of the following uncertainties:

- although the toxicology database for sulfolane is quite extensive, it is not complete;
- chronic studies are lacking or difficult to interpret (*e.g.*, Zhu *et al.*, 1987); and,
- not all potentially serious adverse effects have been investigated.

In summary, a 300-fold safety factor is proposed, consisting of the following:

Interspecies differences:	10-fold
Variability in human sensitivities:	10-fold
Database inadequacies; subchronic-chronic; serious effects concerns:	3-fold

3.5.1.3 Calculation of Tolerable Daily Intake (TDI)

The TDI is calculated using the following formula:

$$TDI = \left(\frac{NOAEL}{Safety\ Factor} \right)$$

Where: TDI = tolerable daily intake;
NOAEL = no-observed-adverse-effect-level (2.9 mg kg^{-1} bw day^{-1}; see Section 3.5.1.1 above);
Safety Factor = 300 (see Section 3.5.1.2 above);

Substituting these values in the above equation, yields 0.0097 mg kg^{-1} bw day^{-1}, which is the human TDI for sulfolane.

3.5.1.4 Bioavailability

Data were not available to derive bioavailability values for sulfolane. As a result, a bioavailability of 100% has been assumed for oral and dermal exposures.

3.5.2 Guideline Development

The absorbed dose from ingestion of sulfolane in source water for drinking was calculated for humans using (US EPA, 1989; CCME, 1996):

$$Dose\ (mg\ kg\ bw^{-1}\ day^{-1}) = \left(\frac{C_w \cdot IR_w \cdot BIO_O \cdot EF}{BW \cdot AT} \right)$$

Where: C_W = concentration of sulfolane in water (mg L^{-1});
IR_W = drinking water ingestion rate (0.6 L day^{-1} (child, 0.5 to 5 years) and 1.5 L day^{-1} (adult); CCME, 2000);
BIO_O = oral bioavailability (1; Table 2.7);
EF = exposure frequency (365 days; assumed);
BW = receptor body weight (16 kg (child, 0.5 to 5 years) and 70.7 kg (adult); CCME, 2000); and,
AT = averaging time (365 days; assumed).

Absorbed dose calculations for drinking water and dermal contact are used to evaluate the relative importance of sulfolane exposure via oral and dermal routes (see dermal contact check below).

The above formula was re-arranged to yield the source water for drinking guidelines (US EPA, 1989; CCME, 1996):

$$Source\ Water\ for\ Drinking\ Guideline\ (mg\ L^{-1}) = \left(\frac{BW \cdot TDI}{IR_w \cdot BIO_O} \right)$$

Where: BW = receptor body weight (16 kg (child, 0.5 to 5 years) and 70.7 kg (adult); CCME, 2000);
TDI = tolerable daily intake (0.0097 mg kg bw^{-1} day^{-1}; Table 2.7);
IR_W = drinking water ingestion rate (0.6 L day^{-1} (child, 0.5 to 5 years) and 1.5 L day^{-1} (adult); CCME, 2000); and,
BIO_O = oral bioavailability (1; Table 2.7).

For a child and an adult, the proposed Interim source water for drinking guidelines are 0.27 mg L^{-1} and 0.46 mg L^{-1}, respectively (Table 3.1).

3.5.3 Dermal Contact Check

To determine if dermal contact was a significant exposure route relative to oral, dermal exposure modelling was conducted following US EPA (1992, 1997). Dermal exposure modelling is concerned with absorption and transport of chemicals through the outer skin layer (stratum corneum) and into the viable epidermis. The stratum corneum is the primary barrier to dermal absorption. This layer consists of a protein (keratin) and lipid matrix that channels chemicals through transcellular (aqueous) and intercellular (lipid) pathways.

The absorbed dose from dermal contact with sulfolane for a child during bathing was calculated using (US EPA, 1992):

$$Dose\,(mg\,kg^{-1}\,bw\,day^{-1}) = \frac{C_w \cdot SA \cdot ET \cdot PC \cdot EF}{BW \cdot AT \cdot 1000}$$

Where: C_W = concentration of sulfolane in water (mg L^{-1});
SA = skin surface area exposed during bathing (7,640 cm^2 95th percentile for whole body for a 3 to 4 year old child; US EPA, 1992);
ET = length of time the skin is in contact with water (0.5 hours day^{-1}; assumed);
PC = chemical specific dermal permeability constant (0.0002 cm $hour^{-1}$ calculated);
EF = exposure frequency (365 days; assumed);
BW = receptor body weight (16 kg; CCME, 2000);
AT = averaging time (365 days; assumed); and,
The value of 1000 was used to convert from cm^3 to L.

The chemical-specific dermal permeability constant (PC) for sulfolane was estimated using (US EPA, 1992):

$$Log\ PC\ (cm\ hour^{-1}) = -2.72 + 0.71 \cdot \log K_{OW} - 0.0061 \cdot MW$$

Where: $\log K_{ow}$ = *n*-octanol-water partition coefficient (-0.4, unitless); and,
MW = molecular weight (120.17 g mol^{-1}).

Using the chemical/physical properties noted above (see also Table 2.2), the estimated dermal permeability constant for sulfolane was 0.0002 cm $hour^{-1}$.

Assuming a sulfolane concentration in water of 1 mg L^{-1}, and assuming a 0.5 hour bath each day, the calculated absorbed dermal dose for a child was 5 x 10^{-5} mg kg^{-1} bw day^{-1}. The calculated absorbed dose for a child drinking water was 0.038 mg kg^{-1} bw day^{-1}, assuming 1 mg L^{-1} sulfolane concentration in the source water for drinking supply. Based on these assumptions, dermal contact provides approximately 0.1% of the oral dose and therefore can be safely disregarded.

3.6 Data Gaps

3.6.1 Freshwater Aquatic Life

The dataset for freshwater aquatic life was sufficient to derive Interim guidelines. For a Full freshwater aquatic life guideline to be developed, the following additional studies would be required:

- two chronic studies on freshwater fish species resident in North America;
- two chronic studies on two invertebrate species from different classes, one of which was a planktonic species resident in North America (*e.g.*, a daphnid); and,
- one study on a freshwater vascular plant or algal species resident in North America.

All the studies for a Full guideline must be of Primary data quality.

3.6.2 Marine Aquatic Life

The dataset for marine aquatic life guideline was not sufficient to derive Interim guidelines. The following additional toxicity tests would be required:

- two acute or chronic studies on different marine fish species, including one temperate species; and,
- one acute or chronic study on a temperate marine invertebrate species from a different class to *Acartia tonsa*.

For a Full marine guideline to be developed, the following additional studies would be required:

- three studies on three species of temperate marine fish of which at least two are chronic;
- two chronic studies on two temperate marine invertebrate species from different classes; and,
- one study on a temperate marine vascular plant or algal species.

All the studies for a Full guideline must be of Primary data quality.

3.6.3 Irrigation

Sufficient data were available to meet the requirements for the irrigation guideline.

3.6.4 Livestock Watering

To comply with the requirements of the Protocol for an Interim livestock watering guideline, the following additional studies would be required:

- two acute or chronic studies on mammalian species raised in Canada, of which one is a livestock species; and,
- one acute or chronic study on an avian livestock species.

In spite of this deficiency, a Preliminary livestock watering guideline was derived, based on laboratory animal studies.

3.6.5 Source Water for Drinking

Available mammalian toxicological data were considered of sufficient quality to derive an Interim source water for drinking guideline.

3.7 Summary of Water Quality Guidelines

Water quality guidelines were calculated for four water uses: freshwater aquatic life, irrigation, livestock watering, and source water for drinking. The recommended guidelines are summarized in Table 3.1.

3.7.1 Freshwater Aquatic Life

The Interim guideline for freshwater aquatic life was calculated to be 50 mg L^{-1}.

3.7.2 Irrigation

Four guidelines were calculated for irrigation. Based on the Protocol, guidelines were calculated for: 1) cereals, tame hays, and pasture crops; and, 2) other crops. For each of these two groups of plants, guidelines were calculated for two soil types: loam and the most sensitive soil in the toxicity testing (poor soil). The guidelines for cereals, tame hays, and pasture crops were 95 mg L^{-1} (loam), and 42 mg L^{-1} (poor soil). For other crops the guidelines were 38 mg L^{-1} (loam), and 8.4 mg L^{-1} (poor soil).

3.7.3 Livestock Watering

Preliminary guidelines for this water use were calculated for dairy cattle and beef cattle, to represent likely agricultural animals. In addition, a guideline was calculated for deer, to assist in evaluating possible risks to other species. The most sensitive species was the dairy cow, for which a guideline of 14 mg L^{-1} was calculated. The reason for the difference in sensitivity between life stages or species is related to how water consumption relates to body weight. In a situation where water was being used for the consumption of a single livestock species other than cattle, typical water ingestion rates and body weight could be used to calculate a species-specific guideline. It should be noted that this guideline was based on studies on laboratory animals using appropriate safety factors; no toxicological information was available for livestock species (either mammalian or avian). Should such data become available in the future, this guideline could be refined.

3.7.4 Source Water for Drinking

Source water for drinking guidelines were calculated for children (0.27 mg L^{-1}) and adults (0.46 mg L^{-1}). If further mammalian toxicological studies become available in the future, this guideline could be refined.

4. CLOSURE

The information presented in this report was produced exclusively for the purposes stated in the Scope of Work. Komex International Ltd. provided this groundwater derivation document for British Columbia Ministry of Water, Land and Air Protection, solely for the purpose noted above, and does not accept any responsibility for the use of this risk assessment for any purpose other than intended or to any third party.

Komex International Ltd. has exercised reasonable skill, care, and diligence to assess the information acquired during the preparation of this report. The methodology used deriving the guidelines in this report is based on current regulatory protocols and current understanding of biological systems, mechanisms of exposure, and toxicological properties of chemicals.

Questions concerning the derivation or use of the guidelines in this report should be directed to Dr. James Sevigny, Mr. Miles Tindal, or Ms. Adele Houston.

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TABLES

Table 2.1. Common Synonyms and Trade Names for Sulfolane

Synonyms	
Bondelane A	Sulpholane
Bondolane A	Sulphoxaline
Cyclic tetramethylene sulfone	Tetrahydrothiofen-1,1dioxide
Cyclotetramethylene sulfone	Tetrahydrothiophene dioxide
Dihydrobutadiene sulfone	Tetrahydrothiophene 1-dioxide
Dihydrobutadiene sulphone	Tetrahydrothiophene-1,1-dioxide
1,1-Dioxide tetrahydrothiofuran	2,3,4,5-Tetrahydrothiophene-1,1-dioxide
1,1-Dioxidetetrahydrothiophene	2,3,4,5-Tetrahydrothiophene-1,1-dioxo
Dioxothiolan	Tetramethylene sulfone
1,1-Dioxothiolan	Thiocyclopentane dioxide
1,1-Dioxothiolane	Thiocyclopentane-1,1-dioxide
Sulfalone	Thiolane-1,1-dioxide
Sulfolan	Thiophane dioxide
Sulfolane	Thiophane 1,1-dioxide
Sulfoxaline	Thiophan sulfone
Sulphalone	Thiophene, 1,1-dioxide-tetrahydro-

Table 2.2. Physical and Chemical Properties for Sulfolane

Property	*Value*	*Units*	*Reference*
CAS registry number	126-33-0		
Molecular formula	$C_4H_8SO_2$		Kirk-Othmer (1999)
Molecular weight	120.17	g/mol	Lide (1996)
Melting point	28.5	° C	Kirk-Othmer (1999)
Boiling point	287.3	° C	Kirk-Othmer (1999)
Specific gravity			
30° C (sulfolane) /30° C (water)	1.266	-	Kirk-Othmer (1999)
100° C (sulfolane) /4° C (water)	1.201	-	Kirk-Othmer (1999)
Flashpoint	165-178	° C	Kirk-Othmer (1999)
Density at 15° C	1.276	g/cm^3	Kirk-Othmer (1999)
Vapour density (air=1)	4.2	g/L	Shell (1976)
Vapour pressure			
20° C	0.01	Mm Hg	Shell Chemicals (1994)
118° C	5	Mm Hg	Verschueren (1996)
150° C	14.53	Mm Hg	Mellan (1977)
160° C	21.55	Mm Hg	Mellan (1977)
200° C	85.23	Mm Hg	Mellan (1977)
210° C	115.1	Mm Hg	Mellan (1977)
260° C	421.4	Mm Hg	Mellan (1977)
n-Octanol-water partition coefficient (K_{ow})	-0.4	log	Travis and Arms (1988)
	-0.77	log	Shell Chemicals (1994)
Organic carbon partition coefficient (K_{oc})	0.07	log	Shell Chemicals (1994)
Henry's law constant	$8.9x10^{-10}$	$Atm/m^3/mole$	Shell Chemicals (1994)
Solubility in water			
20° C	1,266	g/L	Shell Chemicals (1994)
25° C	379, miscible	g/L	Witzaney and Fedorak (1996)
30° C	miscible	g/L	Windholz *et al.* (1983)
pKa	12.9	-log K	Coetzee (1977)
Water soil partition coefficient (K_d)			
Montmorillonite	0.94	L/kg	Luther *et al.* (1998)
Kaolinite	0.18	L/kg	Luther *et al.* (1998)
humus-rich soil	0.099	L/kg	Luther *et al.* (1998)
till	0.14	L/kg	Luther *et al.* (1998)
sandstone, shale/sandstone	0.008-0.079	L/kg	Luther *et al.* (1998)
Dielectric constant	43.3	-	Kirk-Othmer (1999)
Dermal permeability coefficient (K_p)	0.0002	Cm/hour	US EPA (1992)

Table 2.3. Biodegradation Studies for Sulfolane

Study	Concentration [1] (mg L^{-1})	Microcosm Material	Conditions	Nutrients	Temperature (°C)	Lag Time (days)	Biodegradation Rate (mg L^{-1} day)
Bagnall *et al.* (1984)	3,000	na	aerobic	P	17-25	6	330
Salanitro and Langston (1988)	100	Sandy loam	aerobic	N, P	10	14 to 28	(35 to 42) [2]
McLeod *et al.* (1992)	0.6	Acclimated sludge	aerobic	na	na	<1	>1.5
McLeod *et al.* (1992)	1.4	Unacclimated sludge	aerobic	na	na	14	>1.1
Fedorak and Coy (1996)	13	Sandstone	aerobic	N, P	8	3 to 7	4
Fedorak and Coy (1996)	13	Sandstone	aerobic	none	8	<3	1
Fedorak and Coy (1996)	20	Sandstone	aerobic	N,P	26	<3	7.5
Fedorak and Coy (1996)	20	Sandstone	aerobic	none	26	<3	3.8
Fedorak and Coy (1996)	20	Till	aerobic	N,P	8	15	0.7
Fedorak and Coy (1996)	20	Till	aerobic	none	8	22	0.6
Greene *et al.* (1998)	200	Sandstone	aerobic	N, P	8	1.3	31
Greene *et al.* (1998)	200	Sandstone	aerobic	N, P	28	0.7	154
Greene *et al.* (1998)	200	Till	aerobic	N, P	8	7.5	58
Greene *et al.* (1998)	200	Till	aerobic	N, P	28	1.0	110
Greene *et al.* (1998)	200	Sand	aerobic	N, P	8	2.1	46
Greene *et al.* (1998)	200	Sand	aerobic	N, P	28	1.2	118
Greene *et al.* (1998)	200	Sandstone	anaerobic	N, P	8	35	5
Greene *et al.* (1998)	200	Sandstone	anaerobic	N, P	8	34	5
Greene *et al.* (1998)	200	Sand	anaerobic	N, P	8	168	1
Kim *et al.* (1999)	2,000	"Soil"	anaerobic	na	na	na	na
Greene *et al.* (1999) [3]	490	Till	aerobic	none	8	220	0
Greene *et al.* (1999) [3]	490	Till	aerobic	P	8	5	12
Greene *et al.* (1999) [3]	680	Till	aerobic	none	8	220	0
Greene *et al.* (1999) [3]	680	Till	aerobic	P	8	29	7
Greene *et al.* (1999) [3]	0.0024	Wetland sediment	aerobic	none	8	39	7
Greene *et al.* (1999) [3]	0.013	Wetland sediment	aerobic	none	8	25	10

(1) = minimum concentration reported. (2) = reported at half-life in days. (3)= data reported for 2.5 L microcosms. na = not available.
Nutrients: N = nitrogen; P = phosphorous

Table 2.4. Toxicity of Sulfolane to Terrestrial Plants

Species	Scientific Name	Endpoint	Soil Type	NOEC ($mg\ kg^{-1}$)	LOEC ($mg\ kg^{-1}$)	EC_{25} ($mg\ kg^{-1}$)	EC_{50} ($mg\ kg^{-1}$)	Reference
Lettuce	*Lactuca sativa*	root elongation	Till	290	570	1,300	2,200	Komex (1999)
Lettuce	*Lactuca sativa*	germination	Till	570	1,200	1,400	1,800	Komex (1999)
Lettuce	*Lactuca sativa*	emergence	Artificial	944	1,890	1,530	2,690	CAPP (2001)
Lettuce	*Lactuca sativa*	emergence	Loam	5,400	10,800	6,650	9,830	CAPP (2001)
Lettuce	*Lactuca sativa*	emergence	Sand	911	1,820	1,030	1,430	CAPP (2001)
Lettuce	*Lactuca sativa*	emergence	Till	440	940	940	1,410	CAPP (2001)
Lettuce	*Lactuca sativa*	biomass	Artificial	944	1,890	462	1,780	CAPP (2001)
Lettuce	*Lactuca sativa*	biomass	Loam	10,800	>10,800	>10,800	>10,800	CAPP (2001)
Lettuce	*Lactuca sativa*	biomass	Sand	1,820	>1,820	>1,820	>1,820	CAPP (2001)
Lettuce	*Lactuca sativa*	biomass	Till	1,880	>1,880	>1,880	>1,880	CAPP (2001)
Lettuce	*Lactuca sativa*	root length	Artificial	944	1,890	1,370	2,470	CAPP (2001)
Lettuce	*Lactuca sativa*	root length	Loam	2,700	5,400	7,000	9,840	CAPP (2001)
Lettuce	*Lactuca sativa*	root length	Sand	455	911	526	1,070	CAPP (2001)
Lettuce	*Lactuca sativa*	root length	Till	440	940	572	1,260	CAPP (2001)
Lettuce	*Lactuca sativa*	shoot length	Artificial	1,890	3,780	2,520	>3,780	CAPP (2001)
Lettuce	*Lactuca sativa*	shoot length	Loam	21,600	>21,600	>21,600	>21,600	CAPP (2001)
Lettuce	*Lactuca sativa*	shoot length	Sand	455	911	650	>1,820	CAPP (2001)
Lettuce	*Lactuca sativa*	shoot length	Till	940	1,880	1,690	>1,880	CAPP (2001)
Minimum Toxicity Values for Lettuce				***290***	***570***	***462***	***1,070***	

Table 2.4. Toxicity of Sulfolane to Terrestrial Plants (Cont'd)

Species	Scientific Name	Endpoint	Soil Type	NOEC ($mg\ kg^{-1}$)	LOEC ($mg\ kg^{-1}$)	EC_{25} ($mg\ kg^{-1}$)	EC_{50} ($mg\ kg^{-1}$)	Reference
Carrot	*Daucus carota*	emergence	Artificial	3,780	7,550	4,430	6,340	CAPP (2001)
Carrot	*Daucus carota*	emergence	Loam	10,800	21,600	11,600	19,400	CAPP (2001)
Carrot	*Daucus carota*	emergence	Sand	1,820	3,640	2,280	3,430	CAPP (2001)
Carrot	*Daucus carota*	emergence	Till	1,880	3,760	3,410	4,830	CAPP (2001)
Carrot	*Daucus carota*	biomass	Artificial	1,890	3,780	2,560	>7,550	CAPP (2001)
Carrot	*Daucus carota*	biomass	Loam	21,600	>21,600	>21,600	>21,600	CAPP (2001)
Carrot	*Daucus carota*	biomass	Sand	3,640	>3,640	2,770	>3,640	CAPP (2001)
Carrot	*Daucus carota*	biomass	Till	3,760	>3,760	>3,760	>3,760	CAPP (2001)
Carrot	*Daucus carota*	root length	Artificial	944	1,890	1,220	2,390	CAPP (2001)
Carrot	*Daucus carota*	root length	Loam	2,700	5,400	14,100	17,300	CAPP (2001)
Carrot	*Daucus carota*	root length	Sand	455	911	512	1,800	CAPP (2001)
Carrot	*Daucus carota*	root length	Till	440	940	807	2,390	CAPP (2001)
Carrot	*Daucus carota*	shoot length	Artificial	1,890	3,780	4,040	6,780	CAPP (2001)
Carrot	*Daucus carota*	shoot length	Loam	10,800	21,600	11,800	>21,600	CAPP (2001)
Carrot	*Daucus carota*	shoot length	Sand	1,820	3,640	2,420	>3,640	CAPP (2001)
Carrot	*Daucus carota*	shoot length	Till	1,880	3,760	3,070	>3,760	CAPP (2001)
Minimum Toxicity Values for Carrot				***440***	***911***	***512***	***1,800***	

Table 2.4. Toxicity of Sulfolane to Terrestrial Plants (Cont'd)

Species	Scientific Name	Endpoint	Soil Type	NOEC ($mg\ kg^{-1}$)	LOEC ($mg\ kg^{-1}$)	EC_{25} ($mg\ kg^{-1}$)	EC_{50} ($mg\ kg^{-1}$)	Reference
Alfalfa	*Medicago sativa*	emergence	Artificial	3,780	7,550	5,760	8,180	CAPP (2001)
Alfalfa	*Medicago sativa*	emergence	Loam	23,700	47,300	29,800	35,900	CAPP (2001)
Alfalfa	*Medicago sativa*	emergence	Sand	3,640	7,290	4,320	5,740	CAPP (2001)
Alfalfa	*Medicago sativa*	emergence	Till	3,760	7,510	4,180	5,340	CAPP (2001)
Alfalfa	*Medicago sativa*	biomass	Artificial	944	1,890	2,210	>7,550	CAPP (2001)
Alfalfa	*Medicago sativa*	biomass	Loam	23,700	>23,700	>23,700	>23,700	CAPP (2001)
Alfalfa	*Medicago sativa*	biomass	Sand	7,290	>7,290	>7,290	>7,290	CAPP (2001)
Alfalfa	*Medicago sativa*	biomass	Till	3,760	>3,760	>3,760	>3,760	CAPP (2001)
Alfalfa	*Medicago sativa*	root length	Artificial	944	1,890	1,810	3,120	CAPP (2001)
Alfalfa	*Medicago sativa*	root length	Loam	5,920	11,800	8,390	11,100	CAPP (2001)
Alfalfa	*Medicago sativa*	root length	Sand	911	1,820	931	1,490	CAPP (2001)
Alfalfa	*Medicago sativa*	root length	Till	235	440	490	1,530	CAPP (2001)
Alfalfa	*Medicago sativa*	shoot length	Artificial	7,550	>7,550	>7,550	>7,550	CAPP (2001)
Alfalfa	*Medicago sativa*	shoot length	Loam	23,700	>23,700	>23,700	>23,700	CAPP (2001)
Alfalfa	*Medicago sativa*	shoot length	Sand	1,820	3,640	4,200	6,070	CAPP (2001)
Alfalfa	*Medicago sativa*	shoot length	Till	3,760	>3,760	>3,760	>3,760	CAPP (2001)
Minimum Toxicity Values for Alfalfa				***235***	***440***	***490***	***1,530***	

Table 2.4. Toxicity of Sulfolane to Terrestrial Plants (Cont'd)

Species	Scientific Name	Endpoint	Soil Type	NOEC ($mg\ kg^{-1}$)	LOEC ($mg\ kg^{-1}$)	EC_{25} ($mg\ kg^{-1}$)	EC_{50} ($mg\ kg^{-1}$)	Reference
Timothy	*Phleum pratense*	emergence	Artificial	1,890	3,780	2,990	4,630	CAPP (2001)
Timothy	*Phleum pratense*	emergence	Loam	10,800	21,600	14,000	20,000	CAPP (2001)
Timothy	*Phleum pratense*	emergence	Sand	455	911	2,320	3,160	CAPP (2001)
Timothy	*Phleum pratense*	emergence	Till	1,880	3,760	2,150	3,070	CAPP (2001)
Timothy	*Phleum pratense*	biomass	Artificial	7,550	>7,550	3,260	6,730	CAPP (2001)
Timothy	*Phleum pratense*	biomass	Loam	675	1,350	1,050	2,960	CAPP (2001)
Timothy	*Phleum pratense*	biomass	Sand	228	455	384	>3,640	CAPP (2001)
Timothy	*Phleum pratense*	biomass	Till	3,760	>3,760	1,430	2,930	CAPP (2001)
Timothy	*Phleum pratense*	root length	Artificial	472	944	1,030	1,990	CAPP (2001)
Timothy	*Phleum pratense*	root length	Loam	1,350	2,700	4,050	9,350	CAPP (2001)
Timothy	*Phleum pratense*	root length	Sand	455	911	562	911	CAPP (2001)
Timothy	*Phleum pratense*	root length	Till	na	na	na	na	CAPP (2001)
Timothy	*Phleum pratense*	shoot length	Artificial	1,890	3,780	3,310	5,300	CAPP (2001)
Timothy	*Phleum pratense*	shoot length	Loam	5,400	10,800	13,100	18,400	CAPP (2001)
Timothy	*Phleum pratense*	shoot length	Sand	911	1,820	1,530	2,560	CAPP (2001)
Timothy	*Phleum pratense*	shoot length	Till	940	1,880	1,820	3,110	CAPP (2001)
Minimum Toxicity Values for Timothy				***228***	***455***	***384***	***911***	

Notes: na = not available

Table 2.9. Toxicity of Sulfolane to Aquatic Species

Type of Study	Type of Biota	Common Name	Species	Duration	Endpoint	NOEC (mg L^{-1})	LOEC (mg L^{-1})	LC_{50}/EC_{50} (mg L^{-1})	Temperature (°C)	pH (-)	DO (mg L^{-1})	Hardness (mg L^{-1})	Type of Control	Chemical Analysis?	Experimental Design	Protocol	Reference
Primary Freshwater Data																	
acute	vertebrate	rainbow trout	*Oncorhynchus mykiss*	96 hours	survival			1,264	15±1	8.3	na	255	S	Y	S	ECP	CAPP, 2001
acute	invertebrate	sideswimmer	*Hyalella azteca*	96 hours	survival			1,516	23±1	8.3	na	255	S	Y	S	(ECP)	CAPP, 2001
acute	invertebrate	daphnid	*Daphnia magna*	48 hours	survival			1,245	23±1	8.2	8.5-8.7	280	S	Y	S	ECP	Environment Canada, 2003
Secondary Freshwater Data																	
acute	vertebrate	fathead minnow	*Pimephales promelas*	7 days	survival	1,000	>1,000	>1,000	25	6.8-8.4	5.3-8.8	na	S	N	S	ECP	ERAC, 1998
acute	vertebrate	fathead minnow	*Pimephales promelas*	7 days	growth	1,000	>1,000	>1,000	25	6.8-8.4	5.3-8.8	na	S	N	S	ECP	ERAC, 1998
acute	invertebrate	daphnid	*Daphnia magna*	48 hours	survival	-	-	3,274	na	na	na	na	S	N	S	ECP	ERAC, 1998
acute	invertebrate	daphnid	*Daphnia magna*	48 hours	survival	-	-	40	18-22	7.8-8.2	8.6-9.4	168-176	S	N	S	S	Girling, 1987
chronic	invertebrate	daphnid	*Ceriodaphnia dubia*	7 days	survival	500	1,000	>1,000	25	8.0-8.8	6.8-8.0	na	S	N	S	ECP	ERAC, 1998
chronic	invertebrate	daphnid	*Ceriodaphnia dubia*	7 days	reproduction	250	500	635	25	8.0-8.8	6.8-8.0	na	S	N	S	ECP	ERAC, 1998
chronic	plant/alga	green alga	*Selenastrum capricornutum*	72 hours	growth	500	1,000	723	na	na	na	na	S	N	S	ECP	ERAC, 1998
Unacceptable Freshwater Data																	
acute	vertebrate	goldfish	*Carassius auratus*	24 hours	survival	-	-	4,800	na	na	na	na	na	na	na	na	Bridié *et al.* 1979a
acute	vertebrate	mosquito fish	*Gambusia sp.*	96 hours	survival	-	-	1,930	na	na	na	na	na	na	na	na	Shell, 1984a
acute	vertebrate	mosquito fish	*Gambusia sp.*	48 hours	survival	-	-	4,600	na	na	na	na	na	na	na	na	Shell, 1984a
acute	vertebrate	stickleback	*na*	96 hours	survival	-	-	1,760	na	na	na	na	na	na	na	na	Shell, 1984a
acute	vertebrate	stickleback	*na*	48 hours	survival	-	-	1,820	na	na	na	na	na	na	na	na	Shell, 1984a
acute	invertebrate	daphnid	*Daphnia magna*	24 hours	survival	-	-	270	20±2	7.9-8.4	9.0-9.4	180±10	na	N	S	S	Shell 1984b
acute	invertebrate	daphnid	*Daphnia magna*	24 hours	survival	-	-	160	na	na	na	na	na	na	na	S	Shell 1984b
acute	invertebrate	daphnid	*Daphnia magna*	48 hours	survival	-	-	94	20±2	7.9-8.4	9.0-9.4	180±10	na	N	S	S	Shell, 1984b
acute	invertebrate	daphnid	*Daphnia magna*	48 hours	survival	-	-	95	na	na	na	na	na	na	na	S	Shell, 1984b
chronic	invertebrate	daphnid	*Ceriodaphnia dubia*	7 days	reproduction	<375	375	-	na	na	na	na	na	na	na	na	Wong *et al.* 1993
chronic	invertebrate	daphnid	*Ceriodaphnia dubia*	7 days	survival	1,500	3,000	2,575	na	na	na	na	na	na	na	na	Wong *et al.* 1993
chronic	plant/alga	duckweed	*Lemna minor*	4-7 days	growth	-	-	>2,500	na	na	na	na	na	na	na	na	SRC, 1994
chronic	plant/alga	green alga	*Selenastrum capricornutum*	24 hours	^{14}C uptake	-	-	10,000 – 50,000	na	na	na	na	na	na	na	na	SRC, 1994
chronic	plant/alga	green alga	*Selenastrum capricornutum*	72-96 hours	biomass	-	-	>1,000	na	na	na	na	na	na	na	na	SRC, 1994
chronic	plant/alga	green alga	*Selenastrum capricornutum*	96 hours	growth rate	-	-	>1,000	na	na	na	na	na	na	na	na	PSE Dossier, 1993
chronic	other	cyanobacteria	*Aphanizomenon flos-aquae*	24 hours	^{14}C uptake	-	-	500 – 1,000	na	na	na	na	na	na	na	na	SRC, 1994
chronic	other	cyanobacteria	*Aphanizomenon flos-aquae*	24 hours	nitrogen fixation	-	-	5,000 – 10,000	na	na	na	na	na	na	na	na	SRC, 1994
chronic	other	diatom	*Cyclotella meneghiana*	24 hours	^{14}C uptake	-	-	10,000 – 50,000	na	na	na	na	na	na	na	na	SRC, 1994
Secondary Marine Data																	
acute	invertebrate	copepod	*Acartia tonsa*	24 hours	immobilization	-	-	350	18-22	7.8-8.2	6.8-7.8	na	Y	N	F	S	Girling, 1987
acute	invertebrate	copepod	*Acartia tonsa*	48 hours	immobilization	-	-	52	18-22	7.8-8.2	6.8-7.8	na	Y	N	F	S	Girling, 1987
Unacceptable Marine Data																	
acute	invertebrate	oyster	*Crassostrea gigas*	24 hour	na	-	-	460	na	na	na	na	na	na	na	na	Fairhurst *et al.* 1992
acute	other	bacterium (microtox)	*Vibrio fischerii*	na	luminescence	-	-	30	na	na	na	na	na	na	na	na	SRC, 1994
acute	other	bacterium (microtox)	*Vibrio fischerii*	na	luminescence	-	-	59	na	na	na	na	na	na	na	na	ERAC, 1998
chronic	invertebrate	mysid shrimp	*Mysidopsis bahia*	7 day	growth	150	-	-	na	na	na	na	na	na	na	na	Wong *et al.* 1993

Notes
General: - = no data or not applicable, na = not available.
Chemical Analysis?: Y = yes, N = no.
Controls Satisfactory?: S = satisfactory, U = unsatisfactory.
Experimental Design: F = flow through, R = renewal, S = static.
Protocol: ECP = Environment Canada Protocol, (ECP) = Modified Environment Canada Protocol, S = Shell Internal Protocol.

Table 2.6. Acute Toxicity of Sulfolane to Mammalian Species

Species	*Route of Administration*	*LD_{50} (mg kg^{-1} bw)*	*Reference*
Rat	intravenous	1,094	Andersen *et al.*, 1976
	oral	1,846	Andersen *et al.*, 1976
	parenteral	1,598	Andersen *et al.*, 1976
	subcutaneous	1,606	Andersen *et al.*, 1976
	oral	2,504	Zhu *et al.*, 1987
Mouse	intravenous	632	Andersen *et al.*, 1976
	intravenous	1,080	Alexander *et al.*, 1959
	parenteral	1,270	Andersen *et al.*, 1976
	subcutaneous	1,360	Andersen *et al.*, 1976
	oral	2,343	Zhu *et al.*, 1987
Guinea pig	oral	1,815	Andersen *et al.*, 1976
	oral	2,100	Brown *et al.*, 1966
	parenteral	1,331	Andersen *et al.*, 1976
	oral	1,445	Zhu *et al.*, 1987
Rabbit	intravenous	(640-850) [1]	Andersen *et al.*, 1976
	subcutaneous	(1,990-3,500) [1]	Andersen *et al.*, 1976
Mean of all data [2]		**1,540**	
Standard deviation of all data [2]		**550**	

Notes:

(1) not enough animals were used to calculate the LD_{50}, so only a range is given. Animals dosed with less than the lower dose indicated survived; those with more than the upper dose died; and,

(2) the low end of the range presented in the rabbit studies was used to calculate these values.

Table 2.7. Tolerable Daily Intakes of Sulfolane for Humans

NOAEL ($mg\ kg^{-1}\ bw\ day^{-1}$)	*Safety Factor*	*TDI* ($mg\ kg^{-1}\ bw\ day^{-1}$)	*Bioavailability*	
			Oral	*Dermal*
Humans				
2.9	300	0.0097	1.0 (1)	1.0 (1)

(1) = Assumed due to lack of data required to estimate bioavailability

Table 3.1. Water Quality Guidelines for Sulfolane

	Water Use				
	Freshwater Aquatic Life *($mg\ L^{-1}$)*	***Marine Life*** *($mg\ L^{-1}$)*	***Irrigation*** *($mg\ L^{-1}$)*	***Livestock Watering*** *($mg\ L^{-1}$)*	***Source Water for Drinking*** *($mg\ L^{-1}$)*
Limiting Guideline	**50**	-	**8.4**	**14**	**0.27**
Guideline	50	-	Loam: 95 (tame hay, cereal, pasture) 38 (other crops) Poor soil [1]: 42 (tame hay, cereal, pasture) 8.4 (other crops)	14 (dairy cow) 20 (beef cattle) 34 (deer)	0.27
Guideline Status	*Interim*	*Not Available*	*Interim*	*Preliminary*[2]	*n/a*

(1) The "poor soil" guideline is calculated using the species/endpoint/soil type combination that yielded the lowest guideline (see text). In practice, "poor soil" is either till or sand. The "poor soil" guideline is protective of plants growing in all soil types.

(2) Insufficient data to satisfy protocol requirements for an Interim guideline. Guideline generated from mean LC_{50} value of 16 data points included in 4 studies using 4 routes of administration on 4 species of laboratory animals. Guideline is designated "Preliminary".